

Laporan
PROGRAM HIBAH KOMPETITIF PENELITIAN
UNGGULAN STRATEGIS NASIONAL
Tahun Anggaran 2009



**PENGEMBANGAN DAN PEMANFAATAN TANAMAN OBAT
INDONESIA MENJADI PRODUK FITOFARMAKA DENGAN
TEKNOLOGI FITOSOM UNTUK TERAPI TUBERCULOSIS**

Ketua Peneliti :

Idha Kusumawati

Dibiayai oleh Direktorat P Penelitian dan Pengabdian kepada Masyarakat
Direktorat Jenderal Pendidikan Tinggi
Departemen Pendidikan Nasional
Surat perjanjian DP2M No : 734/H3.13/PPd/2009
Tanggal : 31 Juli 2009

Universitas Airlangga
Desember 2009

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MILIK
PERPUSTAKAAN
UNIVERSITAS AIRLANGGA
SURABAYA

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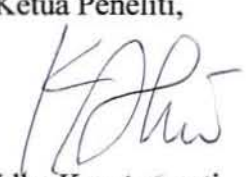
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RINGKASAN

Pengembangan dan pemanfaatan obat bahan alam Indonesia merupakan suatu rangkaian proses yang panjang secara bersama-sama mulai hulu sampai ke hilir dengan memanfaatkan kemajuan teknologi yang berkembang pesat saat ini.

Center for Phytopharmaceutical Development (CPPD), suatu pusat studi pengembangan obat fitofarmaka dari tanaman obat Indonesia yang merupakan suatu pusat riset hasil dari Implementasi Program Hibah Kompetisi B (PHK-B) Fakultas Farmasi Universitas Airlangga, bekerjasama dengan berbagai instansi terkait dan industri obat yang merupakan mitra (*stakeholder*) untuk pengembangan obat fitofarmaka dari hulu ke hilir berbasis teknologi.

Dimulai dengan penelitian di tingkat akademisi, CPPD bersama-sama dengan Institute of Tropical Disease Universitas Airlangga dan RSUD Dr. Soetomo serta Balai Besar Laboratorium Kesehatan Daerah, Surabaya, mengenai peningkatan potensi suatu obat herbal yang selama ini digunakan secara empiris menjadi suatu obat fitofarmaka yang telah terbukti kualitasnya sehingga dapat menjamin keamanan dan khasiat penggunaannya. Kemudian bersama-sama dengan Industri obat, PT. Indofarma melakukan *scale-up* sehingga potensi obat fitofarmaka ini dapat diproduksi dan digunakan dalam pelayanan kesehatan pada masyarakat. Di samping itu untuk mencegah eksploitasi sumber daya alam Indonesia, bersama dengan BALITRO, Departemen Pertanian, melakukan pengembangan budidaya obat herbal yang terstandar yang nantinya dapat dijadikan suatu komoditi pertanian pilihan bagi masyarakat petani.

masyarakat petani.

Obat fitofarmaka adalah suatu sediaan obat bahan alam yang bahan bakunya terstandardisasi serta khasiat dan keamanannya telah terbukti secara klinik. Obat fitofarmaka yang akan dikembangkan ditujukan untuk terapi Tuberculosis (TB) sebab sampai saat ini, di Indonesia, TBC merupakan penyebab kematian utama dan angka kesakitan dengan urutan teratas setelah ISPA. Disamping itu, penelitian awal yang telah dilakukan sebelumnya telah menunjukkan beberapa tanaman obat herbal Indonesia telah terbukti mempunyai aktivitas yang berpotensi untuk terapi TB. Begitu juga mengenai pengembangan metode control kualitas obat herbal yang telah berhasil dilakukan juga merupakan suatu modal untuk pembuatan obat fitofarmaka ini.

Teknologi fitosom adalah suatu teknologi terbaru dalam formulasi obat herbal yang saat ini dikembangkan untuk memperbaiki farmakokinetika bahan aktif obat herbal sehingga akan dapat meningkatkan potensi obat herbal ini, sehingga penelitian ini dapat dijadikan sebagai suatu model pengembangan teknologi fitosom untuk obat herbal.

Pada tahun pertama akan dilakukan validasi pembuktian aktivitas dan keamanan obat fitofarmaka baik pada tingkat preklinik dan validasi metode control kualitas untuk menjamin mutu produk sehingga akan dihasilkan suatu produk yang reproduisibel.

Selanjutnya pada tahun kedua, scale-up di industri obat akan dilakukan setelah seluruh proses penelitian pada skala laboratorium berhasil diselesaikan, sehingga obat fitofarmaka yang dihasilkan oleh industri obat dapat digunakan pada pelayanan kesehatan. Pada tahun kedua juga dilakukan standardisasi proses budidaya sampai pasca

panen sehingga diharapkan nantinya komoditi tanaman obat ini dapat diterapkan pada masyarakat petani dengan suatu proses yang sudah terstandar sehingga hasil yang diperoleh sebagai bahan baku obat herbal mempunyai kualitas yang terstandar, dan juga proses standarisasi ini dapat dijadikan suatu model yang dapat diterapkan pada berbagai tanaman obat sehingga dapat meningkatkan kualitas komoditi tanaman obat sehingga berpeluang untuk masuk dalam skala ekspor.

BAB 1

PENDAHULUAN



1.1.LATAR BELAKANG

Sebagai Negara yang kaya akan keanekaragaman hayati dengan tradisi pemanfaatan tanaman obat untuk kesehatan, sudah selayaknya saat ini masyarakat Indonesia lebih berkembang dalam hal pemanfaatan tanaman obat untuk menanggulangi berbagai masalah kesehatan yang ada seperti halnya China, Korea dan Jepang.

Pengembangan dan pemanfaatan obat bahan alam Indonesia juga harus mampu meningkatkan perekonomian bangsa Indonesia, karena tanaman obat dapat dijadikan komoditi pertanian pilihan bagi masyarakat petani. Di samping itu dapat menyerap tenaga kerja sehingga mengurangi pengangguran.

Sebagaimana diketahui kegiatan produksi, perdagangan dan penggunaan obat bahan alam merupakan rangkaian proses yang panjang mulai dari hulu ke hilir, berupa kegiatan pengumpulan bahan di hutan yang merupakan tanaman liar atau budidaya tanaman obat, pengolahan pasca panen, pengolahan bahan baku, produksi obat jadi, pemasaran dan penggunaannya untuk pemeliharaan kesehatan, pencegahan dan pengobatan penyakit.

Pengembangan obat bahan alam bertujuan untuk menghasilkan suatu produk obat bahan alam yang aman, bermutu dan bermanfaat. Untuk mencapai hal tersebut, suatu program pengembangan obat bahan alam harus dijalankan bersama dari semua aspek mulai dari hulu ke hilir dengan memanfaatkan kemajuan ilmu pengetahuan dan teknologi yang berkembang pesat saat ini.

Arah kebijakan pengembangan obat bahan alam Indonesia telah ditetapkan oleh pemerintah dan dikelompokkan menjadi : 1) Jamu, yaitu sediaan obat bahan alam yang khasiat dan keamanannya telah diketahui secara turun temurun berdasarkan pengamatan empiric; 2) Obat Herbal Terstandar, yaitu sediaan obat bahan alam yang bahan bakunya telah terstandardisasi serta khasiat dan keamanannya telah melalui uji preklinik; dan 3) Obat Fitofarmaka, yaitu sediaan obat bahan alam yang bahan bakunya terstandardisasi serta khasiat dan keamanannya telah terbukti melalui uji klinik.

Tuberkulosis (TB) masih menjadi masalah kesehatan yang mendunia. Penyakit yang disebabkan infeksi kuman *mycobacterium tuberculosis* ini menjadi “pembunuh” nomor satu untuk kategori penyakit infeksi. Di Indonesia TBC merupakan penyebab kematian utama dan angka kesakitan dengan urutan teratas setelah ISPA. Indonesia menduduki urutan ketiga setelah India dan China dalam jumlah penderita TBC di dunia. Jumlah penderita TBC paru dari tahun ke tahun di Indonesia terus meningkat. Saat ini setiap menit muncul satu penderita baru TBC paru, dan setiap dua menit muncul satu penderita baru TBC paru yang menular. Bahkan setiap empat menit sekali satu orang meninggal akibat TBC di Indonesia.

Kendati penyakit ini disebabkan oleh bakteri, namun sistem kekebalan tubuh penderita mempunyai pengaruh yang cukup besar. Karena itu, salah satu bentuk penyembuhannya adalah dengan meningkatkan daya tahan tubuh selain mengobati penyebab penyakit itu. Obat anti TB (OAT) diberikan dalam bentuk kombinasi beberapa jenis obat, dalam jumlah dan dosis yang tepat selama 6-9 bulan supaya kuman dapat dibunuh. Pengobatan TB diberikan dalam 2 tahap, yaitu tahap intensif dan tahap lanjutan. Tahap intensif dimaksudkan untuk

menghentikan proses penyakit. Tahap ini harus dilaksanakan dengan pengawasan ketat untuk mencegah terjadinya kekebalan obat selama 2 bulan. Sedangkan tahap lanjutan dimaksudkan agar semua kuman yang dorman (tidur) terbunuh. Pemberian obat kombinasi lebih sedikit tetapi dalam jangka waktu lebih panjang yaitu 4 bulan.

Peran obat herbal atau obat fitofarmaka yang dikembangkan dari tanaman obat Indonesia diharapkan dapat menjadi adjuvan dalam terapi penyakit TB. Adjuvan dalam terapi ini adalah untuk meningkatkan atau mengoptimalkan hasil terapi diantaranya adalah untuk meningkatkan fungsi dan aktivitas sistem imun sehingga dapat membantu mengeradikasi penyebab terjadinya infeksi. Penggunaan obat herbal yang merupakan adjuvan ini dapat dipadukan bersama-sama dengan OAT. Untuk itu pada penelitian ini pengembangan dan pemanfaatan tanaman obat Indonesia ditujukan untuk terapi TB

Berdasarkan hasil penelitian yang telah dilakukan, dan didukung data-data ethnomedisin, *Centella asiatica* (pegagan), *Morinda citrifolia* (mengkudu) dan *Andrographis paniculata* (sambiloto) merupakan tanaman-tanaman yang menunjukkan potensi untuk dikembangkan menjadi obat fitofarmaka untuk terapi TB, baik secara tunggal maupun kombinasi. Dalam penelitian ini akan dilakukan validasi pembuktian aktivitas dan toksisitasnya sehingga diperoleh suatu bahan, baik tunggal maupun kombinasi dari ketiga tanaman tersebut yang mempunyai aktivitas yang tinggi dan toksisitas yang rendah yang dapat digunakan sebagai bahan aktif obat fitofarmaka untuk terapi TB.

Untuk masing-masing tanaman, CPPD telah berhasil mengembangkan metode analisis yang dapat digunakan sebagai kontrol kualitas berdasarkan kadar

senyawa markernya, penetapan kadar asiaticosida dalam *Centella asiatica*, skopoletin dalam *Morinda citrifolia* dan Andrografolida dalam *Andrographis paniculata*. Metode ini digunakan sebagai kontrol kualitas untuk standardisasi pada proses budidaya sampai pasca panen dalam penyiapan bahan baku/ raw material yang akan digunakan, standardisasi pada proses pembuatan ekstrak sampai proses manufakturing pembuatan produk. Metode ini juga menjadi dasar pengembangan metode analisis untuk menentukan bioavailabilitas produk yang dihasilkan. Pada penelitian ini akan dikembangkan pula suatu metode analisis untuk metabolit profiling sebagai kontrol kualitas dari raw material sampai produk, sebab safety dan efektifitas tidak hanya ditentukan oleh satu senyawa, senyawa marker, saja tapi keseluruhan senyawa yang ada di dalam ekstrak sebagai bahan aktif obat fitofarmaka. Kontrol kualitas dengan menggunakan metabolit profiling ini juga akan menjadi suatu model untuk mengembangkan metode serupa untuk tanaman/ekstrak yang lain.

Pada proses formulasi, akan digunakan teknologi fitosom. Teknologi ini merupakan teknologi baru yang dikembangkan untuk meningkatkan/memperbaiki farmakokinetika dari ekstrak, dengan menggunakan suatu bahan, sehingga produk yang dihasilkan akan menjadi lebih baik.

Standardisasi proses budidaya sampai penanganan pasca panen dimaksudkan agar hasil penelitian yang dihasilkan dapat digunakan untuk pemberdayaan masyarakat dalam meningkatkan jumlah dan kualitas komoditi pertanian tanaman obat sebagai bahan baku untuk memenuhi kebutuhan industri yang akan memproduksi obat fitofarmaka ini.

Proses scale-up dilakukan agar hasil penelitian ini bisa langsung diimplementasikan oleh industri yang terlibat, sehingga dapat segera digunakan dalam pelayanan kesehatan masyarakat. Sedangkan pengujian klinik yang dilakukan agar dapat teregistrasi sebagai obat fitofarmaka merupakan kelanjutan dari penelitian ini sebab harus dilakukan pada tiga sentra pengujian klinik dan ini akan membutuhkan dana yang lebih besar, sehingga sangat dibutuhkan peran pemerintah dan industri untuk dapat menuntaskan hasil riset terpadu yang telah dilakukan.

1.2. PERUMUSAN PERMASALAHAN

Dari uraian di atas dapat dirumuskan suatu permasalahan yang akan diselesaikan dalam penelitian ini yaitu :

1. Bagaimana menyediakan bahan baku / raw material yang berkualitas dan terstandar secara kontinyu sehingga proses produksi di industri tidak terhambat karena ketidaktersediaan bahan baku yang memenuhi syarat ?
2. Bagaimana menentukan bahan aktif baik yang berasal dari ekstrak tanaman tunggal maupun kombinasi yang mempunyai efektifitas dan safety yang sesuai untuk digunakan dalam terapi TB ?
3. Bagaimana mengembangkan metode analisis yang dapat digunakan sebagai control kualitas mulai dari raw material sampai produk, dan dapat digunakan untuk mengukur bioavailabilitas produk ?
4. Bagaimana mengembangkan formula yang menggunakan teknologi fitosom sehingga mendapatkan suatu formula obat fitofarmaka yang terbaik ?

5. **Bagaimana melakukan scale-up dari prototype formula yang dihasilkan dalam skala laboratorium untuk diterapkan dalam skala industri ?**

BAB 2

TINJAUAN PUSTAKA

2.1. Tinjauan tentang Tuberculosis

Mycobacterium genus (*Mycobacteriaceae*) sangat tersebar dengan 85 spesies yang sudah diketahui. Sebagian menyebabkan penyakit pada manusia dan hewan dan yang lainnya tersebar di alam. Tiga penyakit mycobacterial pada manusia yang sangat dikenal adalah penyakit pulmonary utama yaitu Tuberculosis (TB) dan dua penyakit kulit yaitu lepra (*M. leprae*) dan buruli ulcer (*M. ulcerans*).

Tuberculosis adalah salah satu penyakit tertua dan sangat mudah menyebar. TB disebabkan oleh *Mycobacterium tuberculosis* (MTB), dan pada sedikit juga disebabkan oleh *M. bovis* and *M. africanum*, dan berlanjut menjadi penyakit infeksi penting yang secara global menginfeksi sedikitnya sepertiga atau dua milyar populasi dunia. TB adalah penyakit bakteri kronik yang sangat menginfeksi melalui udara dan biasanya menginfeksi paru-paru, meskipun organ lain juga seringkali terlibat. Orang yang sehat mampu mengontrol infeksi melalui respon imun yang kuat, menghentikan perkembangan penyakit tanpa perlu memusnahkan organismenya (McKinney, 2000). Beberapa kasus seringkali asimtomatis tetapi dapat diaktifkan kembali disebabkan karena kondisi yang melemahkan system imun seperti malnutrisi, diabetes, maglinancy dan khususnya AIDS (acquired immunodeficiency syndrome). Penyakit pulmonary juga dapat disebabkan oleh mycobactery yang lain seperti *M. kansasii*, *M. intracellulae*, *M. xenopi* and *M. scroful-aceum* (Czajkowska et al., 2002). Dari semua itu, penyakit yang disebabkan *M. kansasii* lebih berhubungan dengan tingkat imunosupresan

dan perkembangan infeksi dari Human Immunodeficiency Virus (HIV) daripada infeksi yang disebabkan oleh MTB (Canueto-Qintero et al., 2003).

Pada pertengahan tahun 1950an penggunaan antibiotic golongan Streptomyces (streptomycin, rifampin) dan senyawa antimikroba kemoterapeutika (pyrazinamide, ethambutol, isonizid) menjadi epicentral untuk terapi TB. Seringkali digunakan dalam kombinasi untuk mencegah perkembangan resistensi obat selama terapi obat jangka panjang, senyawa-senyawa ini secara dramatic dapat mengurangi insiden penyakit khususnya bila terapi dilakukan dengan pengawasan (Mitnick et al., 2003).

Tetapi, pada awal 1990an terbukti bahwa trend yang menjanjikan ini menjadi berbalik karena beberapa faktor misalnya tingginya tingkat perkembangan berlanjutnya penyakit pulmonary ini dan terjadinya resistensi antibiotic. Kecenderungan ini khususnya terjadi di Asia tenggara, subSaharan Africa dan Europa Timur dimana terdapat penuhnya populasi (khususnya di penjara dan pengguna fasilitas jangka panjang), rendahnya nutrisi, diagnose yang inefektif dan rendahnya kualitas regimen terapi seperti halnya AIDS, semua memberikan kontribusi peningkatan kasus-kasus yang diobservasi. Imigran dari daerah-daerah ini menjadi sumber utama penyebab terjadinya multiple-drug resistant di tempat yang lain. Di Negara berkembang, khususnya populasi yang berada di tengah kota, akibat dari peningkatan kemiskinan juga memberikan kontribusi yang besar. Bila mycobactery yang berada dimana-mana terlibat, terapi menjadi suatu tantangan dan seringkali harus digunakan antibiotic makrolida (clarithromycin atau azithromycin) bersamaan dengan satu atau lebih senyawa antimikroba yang lain seperti ciprofloxacin, ethambutol dan rifabutin. Sayangnya

rifabutin dan clarithromycin dapat berinteraksi dengan protease inhibitor dan rifabutin berinteraksi dengan beberapa non-nucleoside reverse tran-scriptase inhibitor, membuat terapi untuk pasien AIDS semakin sulit (Pablos-Mendez, 1998; WHO, 2003).

Baru akhir-akhir ini dapat diketahui bahwa populasi MTB yang berada pada proses infeksi secara fisiologi adalah heterogen dan senyawa terapeutik yang diseleksi untuk menghambat fase glikolitik tidak bisa menghambat fase lambat dan non-growing yang menonjol di granuloma paru, inilah yang menyebabkan terapi menjadi lebih lama (Bishai, 2000). Pada lingkungan yang terasing, dimana oksigen kosong, putaran glyoxylate terjadi sehingga memungkinkan untuk bertahan disamping terapi jangka panjang. Tidak seperti keterlibatan strain pada beberapa fungsi screening assays, “persisters” ini, yang bervariasi dalam kemampuannya terhadap antibiotic antimikroba, hanya dapat diisolasi dari specimen klinik dan lebih berupa asam lemak daripada karbohidrat. Untuk itu, untuk mencapai resolusi yang sesuai dengan tingkah laku infeksi, diperlukan untuk mengidentifikasi senyawa yang mempengaruhi aspek-aspek tersebut sama halnya dengan target farmakologi yang sesuai yang mempengaruhi dinding sel (Scherman et al., 2003), ketahanan bakteri (faktor-faktor virulensi seperti extracellular repeat protein—Erp) dan mekanisme penghambatan sehingga organism langsung ditangani oleh respon imun dari host (sekelompok gen yang berhubungan dengan dengan pengiriman complex cell wall-associated lipid, phthiocerol dimyco-cerosate, PDIM) (McKinney et al., 2000).

2.2. Senyawa-senyawa yang mempunyai potensi sebagai anti-TB

Senyawa murni yang berasal dari alam baik dari tumbuhan rendah atau tinggi, mikroorganisme dan marine organism mempunyai indikasi sebagai senyawa penghambat aktivitas MTB. Namun potensinya secara farmacetis tidak diketahui dan data-data yang menunjukkan aktivitasnya terhadap mikrobakteri yang berada di human masih kurang.

Hasil awal menunjukkan bahwa tanaman obat yang dikoleksi dari Amazon Peru mempunyai potensi yang berharga sebagai sumber senyawa antimikrona baru. Uji skrining dengan menggunakan virulent human strain H37Rv, tanaman-tanaman ini menunjukkan biorekative terhadap MTB (Lewis et al., 1999; Lewis, 2003). Tanaman menunjukkan 80–100% penghambatan yang signifikan terhadap MTB pada 100 mg/mL (<5%). Ada beberapa alasan mengapa tingkat keberhasilan tanaman-tanaman ini lebih tinggi dibandingkan dengan tanaman yang dikoleksi di tempat lain seperti di Amazon Peru floranya unik, tumbuh di tempat tropis, fitoaleksin yang mengontrol pathogen tanaman yang berhubungan dengan *Streptomyces*. Juga specimen yang digunakan tidak seperti ekstrak tanaman yang digunakan pada awal skrining, specimen ini mengandung senyawa aktif yang sudah didetannified untuk menghilangkan senyawa dengan molekul besar dan sudah di-Cs-sterilized untuk mencegah kontaminasi dari spora bakteri selama proses kultur.

Hasil yang lebih baru 182 ekxtrak yang dipilih secara acak dari semua yang mampu menghambat MTB sebesar 80–100% diuji kemampuannya untuk menghambat konversi dTDP-Glc (thymidine diphospate-a-d-glucose) menjadi dTDP-Rha (deoxythymidine diphosphate rhamnose). Uji mekanisme ini dilakukan

untuk mengidentifikasi penghambatan sintesis dinding sel, target penting dalam industry farmasi. Ini merupakan jalur yang umum untuk MTB dan *M. ulcerans*. Delapan ekstrak menunjukkan aktivitas penghambatan yang kuat dengan IC_{50} (inhibitory concentration 50%) 0.4– ca. 5.0 mg/mL dan 12 yang lain menunjukkan penghambatan yang moderat dengan $IC_{50} >5.0$ mg/mL (Ma et al., 2002 and unpublished).

Review terakhir menunjukkan banyak spesies tanaman yang mempunyai aktivitas anti-mycobacterial activity (Asres et al., 2001; Newton et al., 2002; Cantrell et al., 2001). Begitu juga dengan 39 senyawa marine (Konig et al., 2000). Pada review ini, Newton et al. (2000) melaporkan dari 138 species tanaman dan tidak kurang dari 112 senyawa murni mempunyai aktivitas yang moderat sampai tinggi sebagai antimikroba. Cantrell et al. (2001) juga mereview tentang antimikroba dari terpenoid. Review ini juga menunjukkan keanekaragaman struktur dalam yang mempunyai sifat sebagai antimikroba dengan kemampuan penghambatan minimal (MICs) of <200 mg/mL, termasuk senyawa-senyawa dari golongan yang berbeda seperti alkaloids, terpenoids, coumarins/chromones, peptides and phenolics yang diperoleh dari tanaman, marine, jamur dan bacterium. Ini menjadi perhatian bagi para natural product chemists, synthetic chemists and biochemists untuk mendapatkan senyawa yang nantinya dapat dikembangkan menjadi obat baru.

2.3. Bioassays aktivitas anti-tubercular

Bioassay-directed fractionation adalah proses yang penting untuk mengidentifikasi senyawa aktif dalam ekstrak. Pada program penemuan obat dari

bahan alam, umumnya dilakukan 2 tahap yaitu mengembangkan metode fitokimia untuk mendapat senyawa murni dan mengembangkan metode bioassay untuk mendapatkan hasil pengujian yang valid terhadap virulent *Mycobacterium tuberculosis* in vivo.

2.3.1. Target/target organism

Mycobacterium tuberculosis H37Rv (ATCC 27294) dengan strain virulent yang telah dikarakterisasi dengan baik, mempunyai kecocokan terhadap specimen klinik. Strain ini hanya bias dikerjakan pada biosafety level 3 laboratory (BL-3). Pekerja harus menggunakan protective gear, dan yang terpenting adalah respirator, yang dapat meminimalkan resiko infeksi karena aerosolized *Mycobacterium tuberculosis*. Beberapa peneliti menggunakan virulent strain yang cepat tumbuh, saprophytic mycobacteria yaitu *Mycobacterium smegmatis* (ATCC 607). Organisme ini hanya mempunyai tingkat kesamaan yang kecil terhadap *Mycobacterium tuberculosis* dalam hal kerentanan terhadap obat. Alternatif yang lain adalah virulent strain yang lambat tumbuh yaitu *Mycobacterium tuberculosis* H37Ra (ATCC 25177) atau menggunakan strain yang digunakan untuk vaksin yaitu *Mycobacterium bovis* BCG (ATCC 35743). Organisme ini lebih dekat korelasinya dengan *Mycobacterium tuberculosis* H37Rv daripada bakteri yang cepat tumbuh dalam hal kerentanan terhadap obat maupun komposisi genetiknya.



2.3.2. Uji anti-TB *in vitro*

2.3.2.1. Agardiffusion

Uji dengan menggunakan disk atau sumuran sering digunakan untuk mengevaluasi senyawa bahan alam, tidak secara kuantitatif tetapi dapat menunjukkan penghambatan pertumbuhan pada konsentrasi yang telah diketahui. Kelemahan yang utama metode ini adalah bahwa mycobacteria, kaya akan lipid, dinding selnya hidrofobik seringkali tidak cocok untuk senyawa yang kurang polar. (Connell and Nikaido, 1994).

2.3.2.2. Macro and micro agar dilution

Dapat menentukan MIC dengan menggunakan konsentrasi yang telah diketahui dari ekstrak atau fraksi. Hanya beberapa spesies yang cocok, beberapa mycobacteria termasuk *Mycobacterium tuberculosis* akan tumbuh baik pada Middlebrook 7H11 agar yang diberi oleic acid, albumin, dextrose and catalase. Kelemahannya adalah memerlukan waktu 18 hari untuk dapat mendeteksi pertumbuhan koloni.

2.3.2.3. Micro broth dilution

Pertumbuhan mycobacteria dapat dihitung dengan kekeruhan di media cair, tetapi kecenderung mycobacteria untuk menggumpal menyulitkan pada uji ini. Tambahan lagi ekstrak dapat menutupi kekeruhan sehingga menyulitkan untuk menginterpretasi hasilnya. Penggunaan alamar blue (indicator warna oxidation/reduction) mempercepat uji ini dan meningkatkan sensitifitasnya. Hasil Microplate alamar blue assay (MABA) dapat dibaca secara visual tanpa menggunakan instrument (Franzblau et al., 1998). Tetapi dapat juga diukur dengan secara kuantitatif

dengan menggunakan colourimetrically pada 570nm atau secara fluorimetrically pada 530 nm dan mengukur emisinya pada 590 nm (Collins and Franzblau, 1997). Pembacaan secara non-fluorometric juga dapat dilakukan dengan menggunakan non-proprietary resazurin (Palomino et al., 2002; Martin et al., 2003) atau tetrazolium dyes (Abate et al., 1998; Caviedes et al., 2002; Foongladda et al., 2002). Sehingga metode ini memungkinkan untuk digunakan sebagai metode uji high-throughput anti-TB assays pada micro plates menggunakan micro plate spectrophotometer atau micro plate fluorimeter.

2.3.2.4. *Radiorespirometry*

Pertumbuhan atau penghambatan mycobacteria dapat ditentukan dalam 1 minggu dengan meningkatkan oksidasi [$1\text{-}^{14}\text{C}$] palmitic acid pada media cair Middlebrook 7H12 ke $^{14}\text{CO}_2$ yang dapat diukur pada alat BACTEC 460 (Collins and Franzblau, 1997). Dikarenakan data yang diperoleh adalah kuantitatif maka aktivitas relative dari berbagai sampel dapat dibandingkan dengan menguji hanya pada 1 atau 2 konsentrasi saja dan dapat menentukan persen penghambatan produksi $^{14}\text{CO}_2$ dibandingkan dengan control obat (Cantrell et al., 1998a). Alternatifnya dapat diuji pada berbagai konsentrasi dan MIC dapat ditentukan (Rajab et al., 1998). System klinis yang non-radimetric otomatis menggunakan indicator yang memerlukan oksigen (Sanders et al., 2004), menghasilkan CO_2 (Diaz-Infantes et al., 2000) atau head space pressure (Ruiz et al., 2000) untuk menentukan pertumbuhan atau penghambatan.

2.3.2.5. Reporter gene assays

Alternatif uji yang lain adalah penggunaan reporter genes yang dimasukkan ke dalam plasmid yang mampu menentukan viabilitas bakteri dengan mengukur ekspresi protein floresens atau luminesen yang diperkenalkan. Fluorescent proteins seperti red fluorescent protein (RFP) (Cho et al., 2002) dan green fluorescent protein (GFP) (Collins et al., 1998; Changsen et al., 2003) tidak memerlukan substrat eksogen, mudah dihitung dan ditentukan pertumbuhan atau penghambatan kinetiknya.

2.3.3. Anti-TB in vivo assays

Kandidat senyawa harus mempunyai aktivitas terhadap hewan coba yang terinfeksi TB pada dosis yang aman. Mencit diinfeksi dengan aerosol MTB, setelah beberapa lama mencit akan terinfeksi pada periode aktif (lebih dari satu bulan) (Kelly et al., 1996; Falzari et al., 2005) atau selama plateau phase (Stover et al., 2000) pada akhir bulan. Model hewan coba inilah yang digunakan untuk menentukan kemampuan dari kandidat obat (Nuermberger et al., 2004).

2.4. Tinjauan tentang Kontrol Kualitas Obat Herbal

Obat herbal tradisional telah digunakan secara luas selama ratusan tahun di beberapa negara oriental seperti Cina, Korea, Jepang dan lainnya. Salah satu ciri khasnya adalah menggunakan satu herbal atau beberapa herbal yang diekstraksi dengan air mendidih selama proses dekok. Ini merupakan alasan mengapa kontrol kualitas obat herbal menjadi lebih sulit (WHO, 2000). Meskipun keberadaannya, kelanjutan penggunaannya di hampir seluruh dunia, popularitasnya pada dekade

terakhir ini namun obat tradisional tidak dikenal secara resmi. Kuantitas dan kualitas keamanan dan efektifitasnya jauh dari cukup untuk memenuhi kriteria yang dibutuhkan dalam penggunaannya secara luas. Alasan utamanya adalah kurangnya metodologi penelitian yang dapat diterima untuk evaluasi obat tradisional.

Secara umum, satu atau dua senyawa marker atau senyawa aktif dalam herbal atau campuran herbal digunakan untuk evaluasi kualitas dan keaslian dari obat herbal, identifikasi herbal tunggal atau sediaan obat tradisional dan penentuan kuantitatif komposisi herbal pada produk herbal. Tetapi penentuan ini tidak dapat memberikan gambaran yang lengkap dari produk herbal sebab *multiple constituent* yang bertanggungjawab terhadap efek terapeutik dari produk herbal. *Multiple constituent* ini bekerja secara sinergis dan tidak dapat dipisahkan untuk mendapatkan bagian-bagian yang aktif. Terlebih lagi, senyawa kimia sebagai komponen herbal dalam produk herbal sangat bergantung pada waktu panen, tempat tumbuh, proses pengeringan dan berbagai faktor lain. Tampaknya sangat diperlukan penentuan sebanyak mungkin kandungan fitokimia dalam produk herbal dalam rangka menjamin reliability dan repeatability penelitian farmakologi dan klinik untuk mengetahui bioaktivitasnya dan kemungkinan efek samping dari senyawa-senyawa aktif tersebut yang nantinya akan berpengaruh terhadap kualitas produk herbal. Beberapa teknik kromatografi seperti HPLC, GC, CE dan TLC dapat digunakan untuk tujuan ini. Dengan teknik ini dapat dilihat spektrum kandungan kimia yang lengkap dari senyawa-senyawa aktif yang ada dalam herbal. Konsep fitoekivalendikembangkan di Jerman dengan tujuan untuk menjamin konsistensi dari produk herbal. Mengacu pada konsep ini, profil kimia

seperti profil kromatogram dari produk herbal harus didasarkan dan dibandingkan dengan profil kromatogram produk referens yang telah terbukti keamanan dan efektifitasnya secara klinik. Tambahan lagi di antara berbagai teknik, metode kromatografi sangat dianjurkan untuk menentukan *fingerprint* dari produk herbal.

Fingerprint kromatogram dari obat herbal adalah pola kromatogram dari ekstrak yang mengandung beberapa komponen kimia dari senyawa-senyawa aktif yang umum dan atau yang merupakan ciri khas. Profil kromatogram ini seharusnya dapat digambarkan dari sifat-sifat dasar seperti "integrity" dan "fuzziness" atau "sameness" dan "differences" dari senyawa-senyawa yang ada pada obat herbal yang ditentukan. Diperkirakan bahwa dengan adanya fingerprint kromatogram yang diperoleh, keaslian dan identifikasi dari obat herbal dapat dilakukan dengan akurat (*integrity*) meskipun jumlah atau konsentrasi dari senyawa yang karakteristik tidak sama persis untuk berbagai sampel dari obat herbal ini (*fuzziness*) atau fingerprint kromatogram dapat menunjukkan dengan jelas, baik "sameness" dan "differences" di antara berbagai sampel. Berdasarkan hal tersebut kita seharusnya menerapkan penggunaan multiple constituent dari pada satu atau dua senyawa marker untuk evaluasi kualitas produk herbal

Tetapi di dalam ekstrak obat herbal, terdapat ratusan senyawa yang tidak diketahui dan banyak di antaranya berada dalam jumlah yang kecil. Tambahan lagi adanya variabilitas di antara herbal yang sama. Konsekuensinya adalah mendapatkan fingerprint kromatogram dari herbal atau produk herbal yang mempunyai aktivitas farmakologi dan komponen kimia yang karakteristik bukanlah hal yang mudah. Untungnya kromatografi mempunyai kemampuan pemisahan yang sangat hebat. Lebih jauh lagi adanya penggunaan teknik tandem

atau gabungan seperti HPLC-DAD, GC-MS, CE-DAD, HPLC-MS dan HPLC-NMR akan sangat membantu analisis kualitatif dan bahkan seringkali langsung dapat digunakan untuk elusidasi struktur. Dan jika teknik ini dikombinasikan dengan pendekatan chemometric, gambaran yang lebih jelas akan dapat dikembangkan dari fingerprint kromatogram yang diperoleh. Sehingga tidak dapat dipungkiri lagi bahwa fingerprint kimia akan menjasi alat kontrol kualitas yang utama dari obat herbal (Liang, 2004).

2.4.1. Kromatografi lapis tipis sebagai pilihan untuk mendapatkan fingerprint kromatogram

Secara umum metode kontrol kualitas obat herbal melibatkan pemeriksaan sensory (makroskopi dan mikroskopi) dan pemeriksaan analitik menggunakan teknik instrumental seperti TLC, HPLC, GC-MS, LC-MS, NIR dan spektrofotometer. Sebaliknya metode ekstraksi dan penyiapan sampel juga penting untuk mendapatkan fingerprint yang bagus dari obat herbal. Fokus yang utama adalah membangun fingerprint kromatogram yang reasonabel dan efisien untuk tujuan kontrol kualitas. Herbal tunggal mengandung banyak senyawa, kombinasi herbal akan meningkatkan interaksi senyawa-senyawa tersebut sehingga lebih menyulitkan dalam pembuatan fingerprint kromatogram yang dapat mewakili masing-masing herbal, hal ini harus menjadi pertimbangan yang penting dalam pembuatan fingerprint kromatogram.

KLT/TLC adalah metode pilihan untuk analisis herbal, bahkan hingga saat ini masih banyak dipakai pada berbagai farmakope misalnya American Herbal Pharmacopoeia (AHP), Chinese Drug Monograph and Analysis, Pharmacopoeia

of the People's Republic of China. KLT digunakan sebab merupakan metode yang mudah dan sederhana, relatif lebih sedikit dalam perubahan pemisahan dibandingkan teknik kromatografi yang lain. KLT juga mempunyai keuntungan dapat melakukan analisis banyak sampel dalam waktu yang singkat. Untuk masing-masing lempeng dapat menganalisa lebih dari 30 noda sampel yang dapat dianalisa dalam satu periode. Dengan bantuan analisis gambar dan pengembangan teknik digital, evaluasi similarity di antara berbagai sampel juga memungkinkan.

Keuntungan penggunaan KLT untuk pembuatan fingerprint obat herbal adalah kemudahan, versatility, kecepatan yang tinggi, sensitivitas yang spesifik dan mudahnya penyiapan sampel, sehingga KLT adalah metode yang tepat untuk penentuan kualitas untuk produk herbal (Liang, 2004).

2.4.2. Chemometric

Esensi dari chemometric adalah mengekstraksi informasi kimia yang relevan dengan mengubah data hasil pengukuran menjadi data yang bisa digunakan dan menampilkan hasilnya dalam bentuk yang tidak menyulitkan. Untuk mendapatkan informasi ini, chemometric membutuhkan metode matematika dan statistik. Teknik pengenalan pola adalah suatu bagian dari chemometric yang bertujuan untuk membedakan dua atau lebih kelompok. Biasanya pola ini menunjukkan adanya hubungan di antara senyawa yang ada dalam satu kelompok. Hubungan ini menunjukkan kesamaan di antara satu kelas dan perbedaan dengan kelas yang lain. Dua di antara teknik pengenalan pola yang banyak digunakan saat ini adalah PCA dan PLS-DA. Bagian terpenting dari chemometric adalah data pre-treatment;

informasi kimia yang relevan harus dilakukan dengan berbagai cara misalnya perbedaan konsentrasi atau noise. Informasi yang relevan dapat ditingkatkan menggunakan signal correction atau teknik scaling yang berbeda. Data pre-treatment menjadi bagian utama untuk menghilangkan perbedaan dan untuk scaling dengan menggunakan standart/referens. Pengenalan pola dapat dilakukan dengan satu atau lebih tahapan, biasanya PCA yang pertama digunakan untuk mengeksplorasi suatu set data baru. PCA mempunyai satu keuntungan dibandingkan dengan PLS bila yang dieksplorasi adalah suatu data baru, sebab tidak berubah karena adanya perubahan eksternal. PCA juga dapat menganalisa dan menggambarkan hasil dari suatu set data yang sangat besar sebab mempunyai kemampuan untuk menampilkan hasil yang komprehensif dalam bentuk scater plots. Scater plots dilakukan dengan cara memplot score vector dari suatu PC dengan PC lainnya yang kemudian dapat digunakan untuk mendapatkan hubungandi antara obyek misalnya untuk tujuan klasifikasi. Loading plots dapat digunakan untuk menghubungkan variabel dan menggambarkan kontribusinya pada model.

PLS-DA adalah metode regresi linear yang digunakan untuk mendapatkan hubungan di antara dua data set (x dan Y) dengan tujuan untuk mengelompokkan obyek baru. PLS-DA mirip dengan PCA tapi perbedaannya adalah adanya y -vector, yang mengandung variabel baru. PLS menunjukkan dua PCA bebas, satu untuk x dan satu untuk y yang dihubungkan melalui score vector. Harus dimengerti bahwa PLS-DA sangat berbeda dengan PCA pada data yang sama. Namun keduanya haruslah sama-sama dilakukan validasi sehingga akan diperoleh data yang optimal (Bankefors, 2008).

BAB 3

TUJUAN DAN MANFAAT

3.1. Tujuan

3.1.1. Tujuan Umum

Mengembangkan dan memanfaatkan potensi tanaman obat Indonesia menjadi obat fitofarmakan yang memenuhi persyaratan efikasi, safety dan reproduibel yang dapat diproduksi oleh suatu industri obat, sehingga dapat masuk dalam system pelayanan kesehatan masyarakat, dan dapat meningkatkan kuantitas dan kualitas komoditi pertanian tanaman obat yang tidak hanya dapat memenuhi pasaran dalam negeri tapi juga diekspor ke luar negeri.

3.1.2. Tujuan Khusus

Untuk dapat mewujudkan tujuan umum maka diperlukan tujuan khusus yang lebih detil yang meliputi :

1. Menyediakan bahan baku / raw material yang berkualitas dan terstandar secara kontinyu sehingga proses produksi di industri tidak terhambat karena ketidaktersediaan bahan baku yang memenuhi syarat
2. Menentukan bahan aktif baik yang berasal dari ekstrak tanaman tunggal maupun kombinasi yang mempunyai efektifitas dan safety yang sesuai untuk digunakan dalam terapi TB
3. Mengembangkan metode analisis yang dapat digunakan sebagai control kualitas mulai dari raw material sampai produk, dan dapat digunakan untuk mengukur bioavailabilitas produk

4. Mengembangkan formula yang menggunakan teknologi fitosom sehingga mendapatkan suatu formula obat fitofarmaka yang terbaik
5. Melakukan scale-up dari prototype formula yang dihasilkan dalam skala laboratorium untuk diterapkan dalam skala industri

3.2. Manfaat

Dari hasil penelitian ini akan dihasilkan suatu prototype bahan baku/raw material yang terstandard, prototype ekstrak terstandard, prototype produk yang terstandard, dan suatu standard operating prosedur mulai dari penyediaan raw material sampai produk. Selain itu juga dari hasil penelitian akan dapat dihasilkan suatu publikasi internasional dan monografi dari raw material dan bahan aktif obat fitofarmaka yaitu ekstrak terstandard. Selain itu akan dapat diproduksi suatu obat fitofarmaka oleh industri obat sehingga dapat digunakan dalam system pelayanan kesehatan masyarakat serta dapat meningkatkan kuantitas dan kualitas komoditi pertanian tanaman obat sehingga dapat memenuhi kebutuhan nasional maupun internasional.

BAB 4

METODE PENELITIAN

4.1. Sampling hasil budidaya

Kegiatan-kegiatan yang dilakukan meliputi kegiatan lapang dan laboratorium, pengambilan bahan baku di area produksi, penelitian mengenai kandungan bahan aktif. Untuk jenis tanaman obat yang sudah dibudidaya secara massal (Mengkudu/noni.) akan diambil di sentra produksi. Untuk Jenis tanaman obat yang belum dibudidayakan (Sambiloto dan Pegagan) akan diambil di daerah produksi (tanaman koleksi Balitro) yang sudah menerapkan *SOP/Standart Operational Pracices* budidaya, sehingga bahan dapat memenuhi kriteria standar Good Agricultural Practices (GAP) dan Good Collection Practices (GACP) sesuai ketentuan WHO (2003) . Semua jenis akan diambil dari minimal 3 (tiga) daerah produksi yaitu :

- a. Pengambilan bahan baku di sentra produksi noni, minimal 3 lokasi. KP. Manoko, Lembang, KP. Cicurug, Sukabumi , KP. Suka Mulia, Sukabumi dan KP. Cimanggu, Bogor

Tanaman ditentukan dengan batasan mempunyai Populasi minimum 10 pohon yang sudah berproduksi, sampel buah diambil dan dilakukan analisa mutu. Dari tanaman yang mempunyai mutu tertinggi yang ditentukan akan dijadikan bahan baku.

- b. Pengambilan bahan baku Sambiloto dan Pegagan, akan digunakan dari tanaman koleksi kebun BALITTRO, dari menggunakan aksesori Nomor Unggul Harapan (Varietas yang akan dilepas). Minimal 3 lokasi, KP. Manoko, Lembang, KP. Cicurug, Sukabumi, KP. Gunung Putri, Cianjur dan KP. Cimanggu, Bogor.

4.2. Ekstraksi

Serbuk kering simplisia ditimbang \pm 200 g, kemudian direfluks dengan penurunan tekanan dengan 2,5 liter pelarut (alkohol 96%, alkohol 70%, alkohol 50% dan air) selama 3 jam dan diulangi 3 kali. Cairan disaring hingga didapatkan ekstrak cair, diuapkan dengan menggunakan vakum evaporator sampai didapatkan ekstrak kental, diuapkan sampai kering. Dan hasilnya adalah sebagai berikut :

4.3. Penetapan kadar senyawa marker

PROSEDUR PENETAPAN KADAR SCOPOLETIN DALAM EKSTRAK MENGGUDU (dengan Metode KLT-Densitometri):

a. Pembuatan dan penjenjahan eluen:

1. Eluen dibuat dari campuran Eter : Toluena : Asam Asetat 10% (22 : 18 : 6 tetes) dengan volume disesuaikan ukuran chamber.
2. Eluen yang telah dibuat kemudian dimasukkan dalam chamber, ditutup dan dibiarkan hingga jenuh.

b. Pembuatan larutan standar skopoletin:

1. Ditimbang 2,0 mg standar skopoletin dan dilarutkan dalam 4,0 ml metanol, sehingga diperoleh kadar 500 ppm (larutan baku induk).
2. (1) diencerkan untuk mendapatkan larutan baku kerja dengan kadar 10, 20, 40, 160, dan 300 ppm.

c. Pembuatan larutan sampel ekstrak buah mengkudu:

1. Ditimbang 200,0 mg sampel ekstrak mengkudu.
2. (1) dimasukkan ke dalam labu ukur 5,0 ml dan ditambahkan metanol hingga tepat 5,0 ml (bila perlu disonikasi untuk melarutkan).

Dilakukan replikasi tiga kali.

d. Penotolan larutan dan penetapan kadar skopoletin:

1. Disiapkan plat KLT dengan ukuran disesuaikan jumlah penotolan.
2. Larutan standar ditotolkan sebanyak 2 μ l, sedangkan sampel ditotolkan sebanyak 20 μ l.
3. Plat KLT yang telah ditotol kemudian dieluasi pada chamber yang sudah jenuh eluennya.
4. Kemudian plat KLT diamati di bawah sinar UV dan dipayar dengan densitometer pada panjang gelombang 346 nm.
5. Ditentukan persamaan regresi linier larutan baku kerja, kadar skopoletin dalam sampel ditentukan dengan mengintrapolasikan luas area noda sampel pada persamaan regresi linier tersebut.

PROSEDUR PENETAPAN KADAR ANDROGRAFOLID DALAM EKSTRAK SAMBILOTO (dengan Metode KLT-Densitometri):

a. Pembuatan dan penjenuhan eluen:

1. Eluen dibuat dari campuran Chloroform : Methanol (9 : 1) dengan volume disesuaikan ukuran chamber.
2. Eluen yang telah dibuat kemudian dimasukkan dalam chamber, ditutup dan dibiarkan hingga jenuh.

b. Pembuatan larutan standar skopoletin:

1. Ditimbang 2,0 mg standar andrografolid dan dilarutkan dalam 4,0 ml metanol, sehingga diperoleh kadar 500 ppm (larutan baku induk).

2. (1) diencerkan untuk mendapatkan larutan baku kerja dengan kadar 10, 20, 40, 160, dan 300 ppm.
3. Pembuatan larutan sampel ekstrak sambiloto
4. Ditimbang 200,0 mg sampel ekstrak sambiloto
5. (1) dimasukkan ke dalam labu ukur 5,0 ml dan ditambahkan metanol hingga tepat 5,0 ml (bila perlu disonikasi untuk melarutkan).

Dilakukan replikasi tiga kali.

c. Penotolan larutan dan penetapan kadar andrografolid:

1. Disiapkan plat KLT dengan ukuran disesuaikan jumlah penotolan.
2. Larutan standar ditotolkan sebanyak 2 μ l, sedangkan sampel ditotolkan sebanyak 20 μ l.
3. Plat KLT yang telah ditotol kemudian dieluasi pada chamber yang sudah jenuh eluennya.
4. Kemudian plat KLT diamati di bawah sinar UV dan dipayar dengan densitometer pada panjang gelombang 230 nm.
5. Ditentukan persamaan regresi linier larutan baku kerja, kadar skopoletin dalam sampel ditentukan dengan mengintrapolasikan luas area noda sampel pada persamaan regresi linier tersebut.

4.4. Uji bioaktivitas antimikroba

Uji bioaktivitas antimikroba dengan menggunakan *Mycobacterium tuberculosis* secara in vitro dengan menggunakan metode dilusi dan masa inkubasi selama 8 minggu.

Pengujian ini sangat dipengaruhi warna dari ekstrak yang digunakan. Untuk itu dilakukan fraksinasi dari ekstrak untuk membebaskan ekstrak dari klorofil (pegagan dan sambiloto) dan untuk membebaskan gula (mengkudu). Fraksinasi menggunakan kolom kromatografi dengan kondisi sebagai berikut :

Fase diam : ion exchange

Fase gerak : gradien (heksan-etil asetat-metanol-air)

4.5. Pengujian toksisitas akut ekstrak terpilih

Penyiapan hewan coba

Hewan coba diaklimatisasi selama 1 minggu, sebelum digunakan untuk uji dipuasakan selama kurang lebih 16 jam, dibagi menjadi 4 kelompok yang masing-masing terdiri 10 ekor jantan dan 10 ekor betina.

Perlakuan untuk masing-masing ekstrak dan campuran ekstrak

Kelompok 1 : diberi ekstrak dengan dosis 200 mg/Kg BB

Kelompok 2 : diberi ekstrak dengan dosis 1500 mg/Kg BB

Kelompok 3 : diberi ekstrak dengan dosis 10000 mg/Kg BB

Kelompok 4 : diberi suspensi CMCNa 0,5% sejumlah yang sama dengan yang diberikan kepada kelompok lain (sebagai kelompok kontrol)

Pelaksanaan

a. Setiap hewan coba diberi ekstrak sesuai dengan dosis masing-masing

b. Setelah 24 jam diamati perilaku dan tanda toksik. Apabila terdapat kematian, dicatat jumlahnya dan diperiksa keadaan organ dalamnya

c. Selanjutnya hewan coba yang ,masih hidup diamati, sekurangnya 7 hari meliputi penurunan berat badan atau perubahan perilaku hewan coba dan apabila ada kematian

4.6. Pembuatan profil metabolit

Pembuatan profil metabolit dilakukan dengan menggunakan metode Kromatografi Lapis Tipis dengan menggunakan Linomat V, Camag scanner III, ADC, Win Cats III dengan

4.7. Formulasi Fitosom

Pembuatan Kompleks Fosfolipid Ekstrak Sambiloto:

1. Ditimbang Ekstrak 500 mg (~ 75 mg andrografolid) dan Phospholipid 250 mg (~75 mg Phosphatidylcholine) dengan rasio molar 1:1
2. Kedua bahan dilarutkan dalam etanol absolute 100 ml menggunakan labu alas bulat, kec. pengadukan (stirring) 60 rpm, suhu 30°C sampai larut sempurna (± 30 menit)
3. Buang solvent dengan rotavapor; kec. putaran 60 rpm, suhu 40°C, tekanan < 1 atm
4. Endapan di-freeze drying selama 1 malam (12 jam)
5. Serbuk kering diambil dan disimpan dalam desiccators atau vacuum oven pada suhu 50°C selama 1 jam
6. Serbuk digerus dan di ayak menggunakan pengayak mesh 100 (ukuran diameter pengayak 180 μm)

7. Sampel dimasukkan dalam botol kaca, dialiri gas nitrogen dan disimpan dalam desiccators pada suhu kamar
8. Karakterisasi menggunakan SEM, TEM, DTA, X-ray

BAB 5**HASIL DAN PEMBAHASAN****5.1. Sampling tanaman budidaya**

Hasil yang diperoleh dari pengambilan sampel adalah 9 simplisia yaitu 3 tanaman yang berasal dari 3 lokasi budidaya yaitu :

1. Mengkudu berasal dari Suka Mulya, Cicurug dan Cimanggu
2. Pegagan berasal dari Manoko, Cicurug dan Gunung Putri
3. Sambiloto berasal dari Cibinong, Cicurug dan Cimanggu

5.2. Rendemen ekstrak

Hasil ekstraksi yang diperoleh adalah sebagai berikut :

Tabel 5.1. Hasil ekstrak Mengkudu

Ekstrak	Suka Mulya		Cicurug		Cimanggu	
	Berat simplisia	rendemen	Berat simplisia	rendemen	Berat simplisia	rendemen
Air	198 g	21,5 %	202,3 g	23,1 %	197,6 g	21,7 %
Alkohol 50%	201,1 g	18,0 %	199,1 g	18,2 %	200,0 g	19,7 %
Alkohol 70%	197,4 g	19,1 %	195,3 g	19,0 %	194,9 g	15,4 %
Alkohol 96%	211,2 g	20,9 %	200,0 g	20,5 %	203,7 g	17,8 %

Rendemen ekstrak terbesar diperoleh dari ekstrak air mengkudu dari Cicurug dan yang terkecil diperoleh dari ekstrak etanol 96% mengkudu dari Cimanggu.

Tabel 5.2. Hasil ekstrak Sambiloto

Ekstrak	Cibinong		Cicurug		Cimanggu	
	Berat simplisia	rendemen	Berat simplisia	rendemen	Berat simplisia	rendemen
Air	201,7 g	22,4 %	189,4 g	20,1 %	135,2 g	15,3 %
Alkohol 50%	198,4 g	18,2 %	195,3 g	17,8 %	112,1 g	12,5 %
Alkohol 70%	203,2 g	19,6 %	180,2 g	17,3 %	135,3 g	13,1 %
Alkohol 96%	215,3 g	20,3 %	194,7 g	44,3 %	92,6 g	27,8 %

Rendemen ekstrak terbesar diperoleh dari ekstrak etanol 96% Sambiloto dari Cimanggu dan yang terkecil diperoleh dari ekstrak etanol 50% sambiloto dari Cimanggu.

Tabel 5.3. Hasil ekstrak Pegagan

Ekstrak	Manoko		Cicurug		Gunung putri	
	Berat simplisia	rendemen	Berat simplisia	rendemen	Berat simplisia	rendemen
Air	210,0 g	23,1 %	170,3 g	19,1 %	150,3 g	17,5 %
Alkohol 50%	200,3 g	19,7 %	185,2 g	17,4 %	157,2 g	15,2 %
Alkohol 70%	201,1 g	19,3 %	190,3 g	18,3 %	165,2 g	16,3 %
Alkohol 96%	206,6 g	19,6 %	167,4 g	15,2 %	170,3 g	18,0 %

Rendemen ekstrak terbesar diperoleh dari ekstrak air pegagan dari Manoko dan yang terkecil diperoleh dari ekstrak etanol 50% pegagan dari Gunung Putri.

5.3. Penetapan kadar senyawa marker

Penetapan kadar senyawa marker dilakukan dengan menggunakan metode KLT-densitometer

Tabel 5.4. Kadar scopoletin dalam ekstrak Mengkudu

Ekstrak	Suka Mulya	Cicurug	Cimanggu
Air	0,0265 %	0,0093 %	0,0061 %
Alkohol 50%	0,0965 %	0,0519 %	0,0491 %
Alkohol 70%	0,0891 %	0,0533 %	0,0550 %
Alkohol 96%	0,0172 %	0,0084 %	0,0108 %

Kadar scopoletin terbesar terdapat dalam ekstrak alkohol 50% mengkudu dari Suka Mulya dan kadar scopoletin terkecil terdapat di dalam ekstrak air mengkudu dari Cimanggu.

Tabel 5.5. Kadar Andrografolid dalam ekstrak Sambiloto

Ekstrak	Cibinong	Cicurug	Cimanggu
Air	1,364 %	1,95 %	1,8 %
Alkohol 50%	9,9 %	11,45 %	9,76 %
Alkohol 70%	22,92 %	11,87 %	14,25 %
Alkohol 96%	9,77 %	6,8 %	4,87 %

Kadar andrografolid terbesar terdapat dalam ekstrak alkohol 70% sambiloto dari Cibinong dan kadar andrografolid terkecil terdapat di dalam ekstrak air sambiloto dari Cibinong.

Dari hasil penetapan kadar senyawa marker dipilih ekstrak yang mempunyai kadar marker terbesar yaitu ekstrak alkohol 50% mengkudu sukamulya, ekstrak alkohol 70% sambiloto Cibinong dan ekstrak alkohol 96% pegagan Manoko. Ketiga ekstrak inilah yang kemudian akan dilakukan uji bioaktivitas dan formulasi.

5.4. Hasil Fraksinasi

Fraksinasi dilakukan menggunakan ion exchange untuk memisahkan klorofil untuk ekstrak pegagan dan sambiloto dan untuk memisahkan gula pada ekstrak mengkudu. Hasilnya adalah sebagai berikut :

5.5. Uji bioaktivitas antimikrobakterium TB in vitro

Pengujian bioaktivitas antimikrobakterium dengan menggunakan *M tuberculosis* dilakukan dengan metode dilusi dengan waktu inkubasi 8 minggu. Pengujian ini sangat dipengaruhi warna dari ekstrak untuk itu dilakukan pemisahan klorofil dari ekstrak sambiloto dan pegagan juga pemisahan gula dari ekstrak mengkudu. Pemisahan ini baru dapat diselesaikan minggu kemarin sehingga pengujian bioaktivitas baru akan dilakukan pada minggu ini.

5.6. Uji toksisitas akut ekstrak terpilih

Hasil uji toksisitas akut ekstrak alkohol 50% mengkudu sukamulya

Tabel 5.6. Jumlah mencit jantan dan betina yang mati pada pengamatan selama 24 jam setelah pemberian oral ekstrak alkohol 50% mengkudu sukamulya dosis tunggal

Kelompok	N	Jumlah kematian
Kontrol	20	0
D200	20	0
D1500	20	0
D10000	20	0

Dari hasil pemeriksaan jumlah kematian untuk menentukan LD50 diketahui bahwa sampai pada pemberian dosis terbesar 10000 mg/kg BB mencit tidak terjadi kematian, sehingga tidak diperoleh nilai LD50 sehingga dapat dikatakan ekstrak alkohol 50% mengkudu sukamulya relatif aman.

Pengamatan dilanjutkan sampai hari ke-7 untuk melihat kegaja toksik yang muncul.

Tabel 5.7. Pengamatan gejala toksik sampai hari ke-7 setelah pemberian oral ekstrak alkohol 50% mengkudu sukamulya dosis tunggal

Efek yang diamati	Kontrol (-) (N=6)				D200 (N=6)				D1500 (N=6)				D10000 (N=6)			
	1	3	5	7	1	3	5	7	1	3	5	7	1	3	5	7
Hari ke																
Pernafasan	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kejang	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Writhing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpitasi cardiac	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Refleks mata	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Defekasi	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Urinasi	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Reaksi terhadap rangsang	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Hasil pengamatan gejala toksik (pada tabel di atas) menunjukkan tidak terlihat adanya gejala toksik pada semua hewan coba.

Hasil uji toksisitas akut ekstrak alkohol 70% sambiloto cibinong

Tabel 5.8. Jumlah mencit jantan yang mati pada pengamatan selama 24 jam setelah pemberian oral ekstrak alkohol 70% sambiloto Cibinong dosis tunggal

Kelompok	N	Jumlah kematian
Kontrol	10	0
D200	10	0
D1500	10	0
D10000	10	0

Dari hasil pemeriksaan jumlah kematian untuk menentukan LD50 diketahui bahwa sampai pada pemberian dosis terbesar 10000 mg/kg BB mencit tidak terjadi kematian, sehingga tidak diperoleh nilai LD50 sehingga dapat dikatakan ekstrak alkohol 50% mengkudu sukamulya relatif aman.

Pengamatan dilanjutkan sampai hari ke-7 untuk melihat kegaja toksik yang muncul.

Tabel 5.9. Pengamatan gejala toksik sampai hari ke-7 setelah pemberian oral ekstrak alkohol 50% mengkudu sukamulya dosis tunggal

Efek yang diamati	Kontrol (-) (N=6)				D200 (N=6)				D1500 (N=6)				D10000 (N=6)			
	1	3	5	7	1	3	5	7	1	3	5	7	1	3	5	7
Pernafasan	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kejang	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Writhing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpitasi cardiac	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Refleks mata	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Defekasi	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Urinasi	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Reaksi terhadap rangsang	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Hasil pengamatan gejala toksik (pada tabel di atas) menunjukkan tidak terlihat adanya gejala toksik pada semua hewan coba.

Hasil uji toksisitas akut ekstrak alkohol 96% pegagan Manoko

Tabel 5.10. Jumlah mencit jantan yang mati pada pengamatan selama 24 jam setelah pemberian oral ekstrak alkohol 96% pegagan Manoko dosis tunggal

Kelompok	N	Jumlah kematian
Kontrol	10	0
D200	10	0
D1500	10	0
D10000	10	0

Dari hasil pemeriksaan jumlah kematian untuk menentukan LD50 diketahui bahwa sampai pada pemberian dosis terbesar 10000 mg/kg BB mencit tidak terjadi kematian, sehingga tidak diperoleh nilai LD50 sehingga dapat dikatakan ekstrak alkohol 50% mengkudu sukamulya relatif aman.

Pengamatan dilanjutkan sampai hari ke-7 untuk melihat gejala toksik yang muncul.

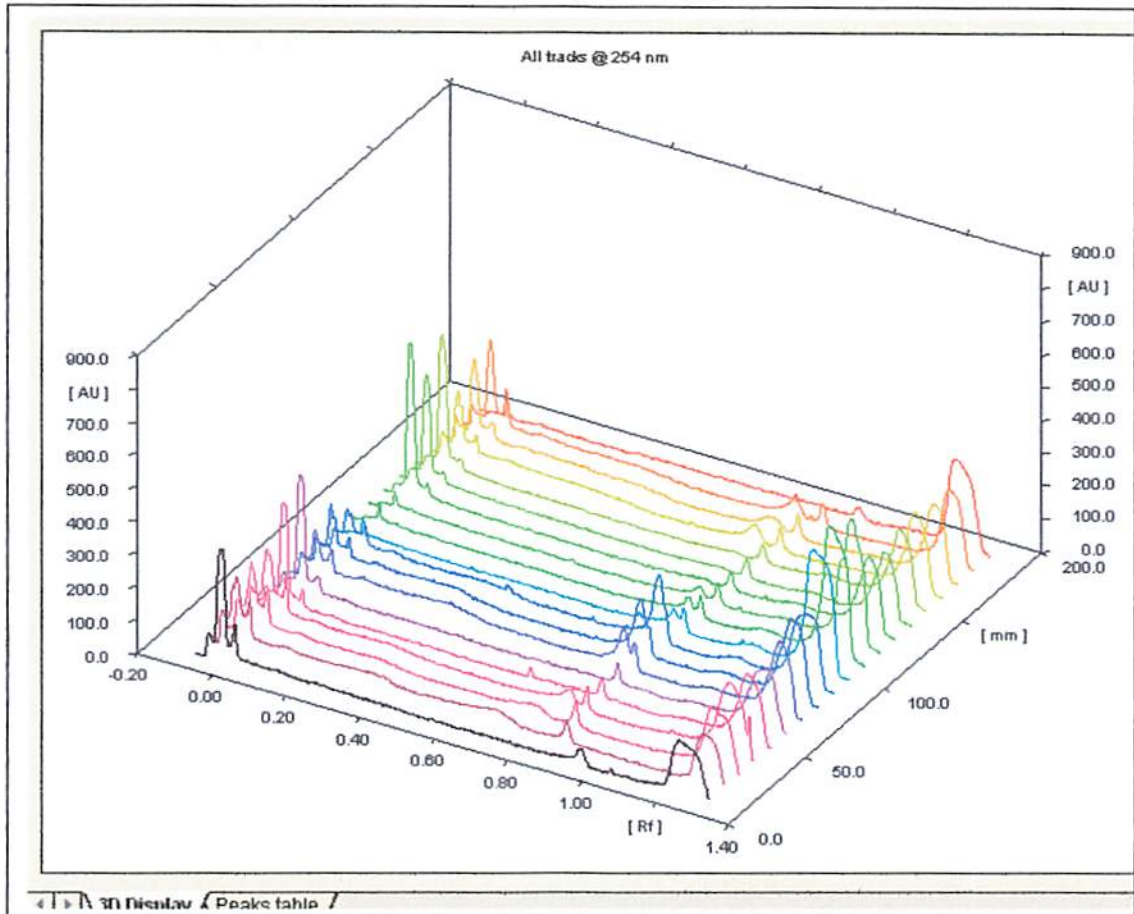
Tabel 5.11. Pengamatan gejala toksik sampai hari ke-7 setelah pemberian oral ekstrak alkohol 96% pegagan Manoko dosis tunggal

Efek yang diamati	Kontrol (-) (N=6)				D200 (N=6)				D1500 (N=6)				D10000 (N=6)			
	1	3	5	7	1	3	5	7	1	3	5	7	1	3	5	7
Pernafasan	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Tremor	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Kejang	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Writhing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Palpitasi cardiac	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Refleks mata	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Defekasi	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Urinasi	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
Reaksi terhadap rangsang	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N

Hasil pengamatan gejala toksik (pada tabel di atas) menunjukkan tidak terlihat adanya gejala toksik pada semua hewan coba.

5.7. Profil metabolit untuk kontrol kualitas

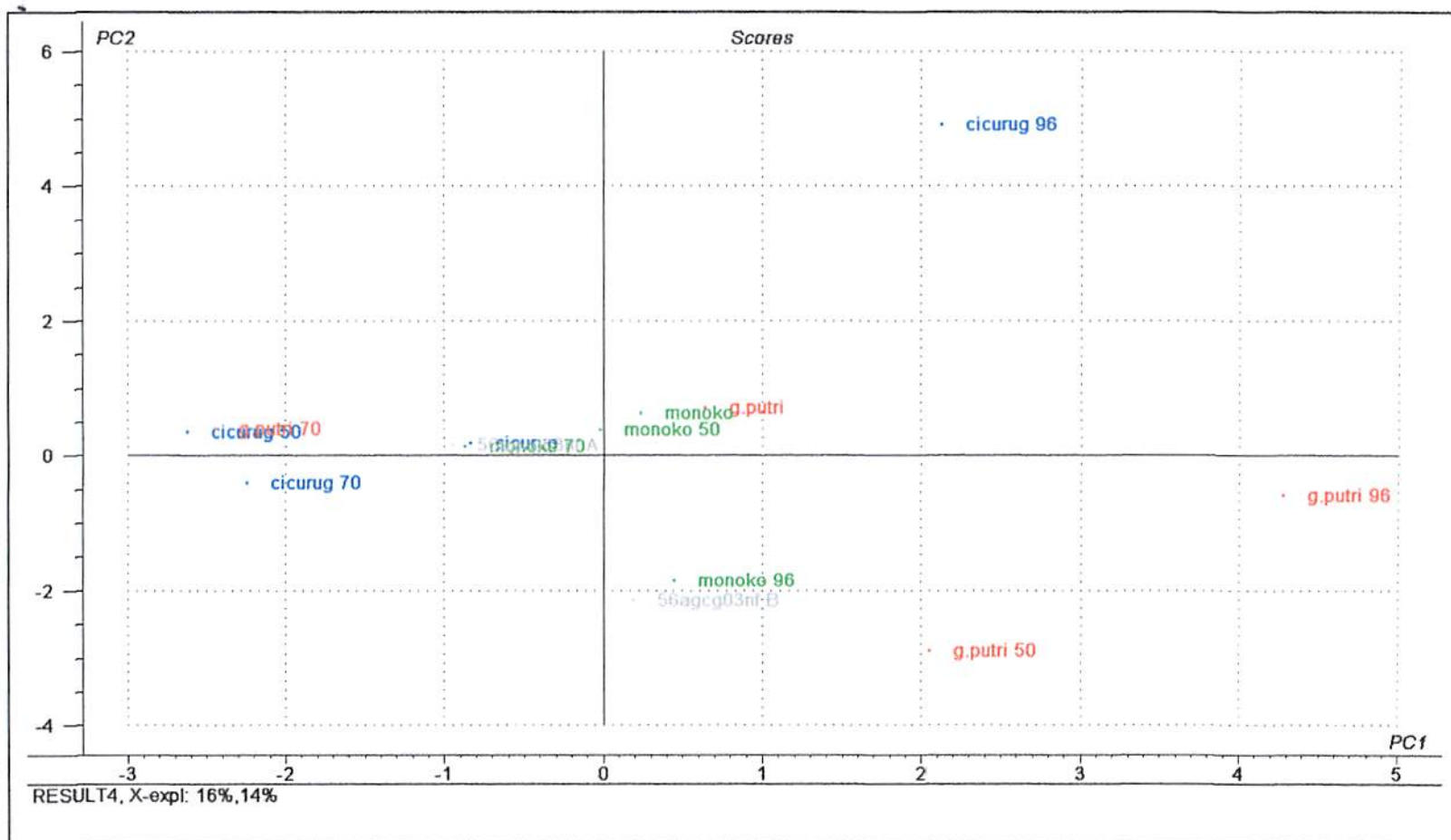
Tiap tanaman menghasilkan 12 ekstrak yaitu tanaman yang diperoleh dari 3 lokasi dan masing-masing diekstraksi dengan 4 macam pelarut yang berbeda.



Gambar 5.1 Profil kromatogram ekstrak pegagan

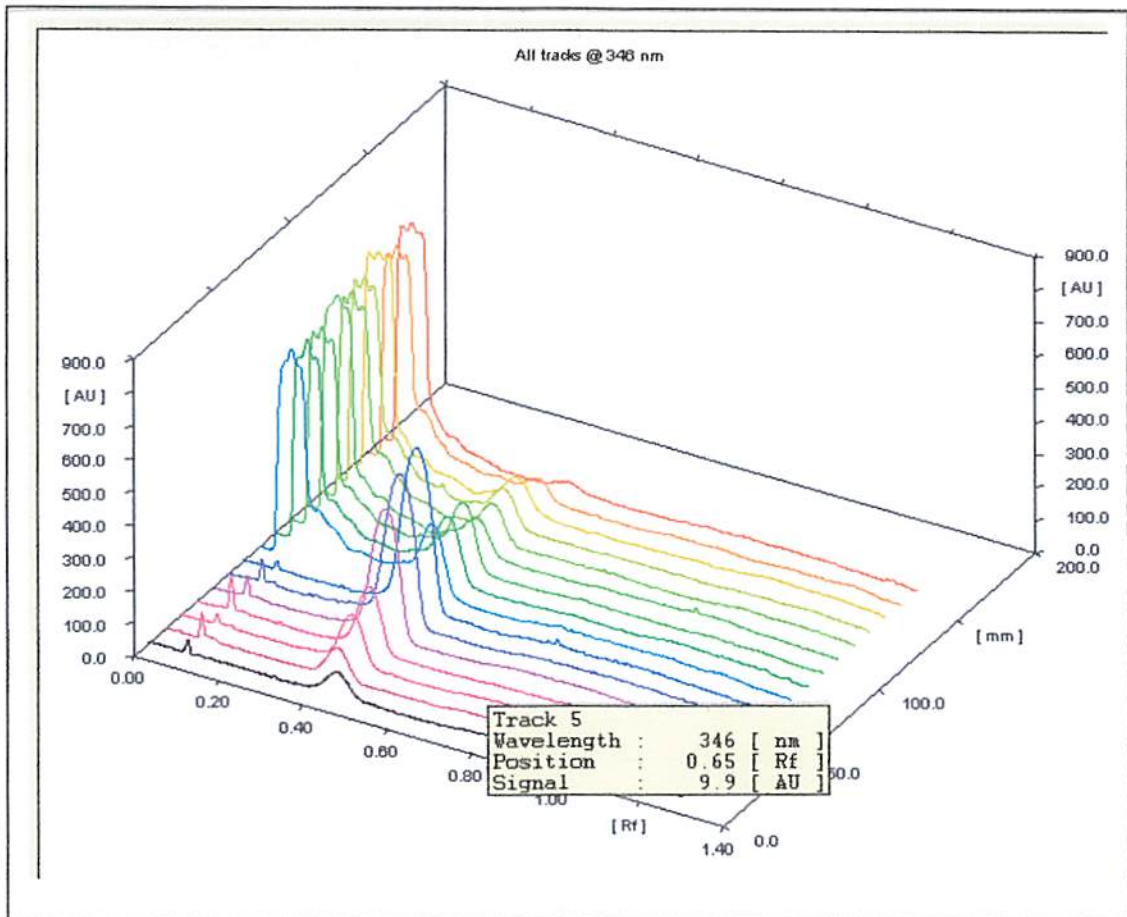
Dari data area masing-masing peak pada kromatogram masing-masing ekstrak dilakukan preprosesing data yang meliputi peak elignment dan normalisasi setelah itu dilakukan uji statistik menggunakan PCA dan PLS.

Hasil uji statistik menggunakan PCA adalah sebagai berikut :



Gambar 5.2. Score plot profil kromatogram ekstrak pegagan

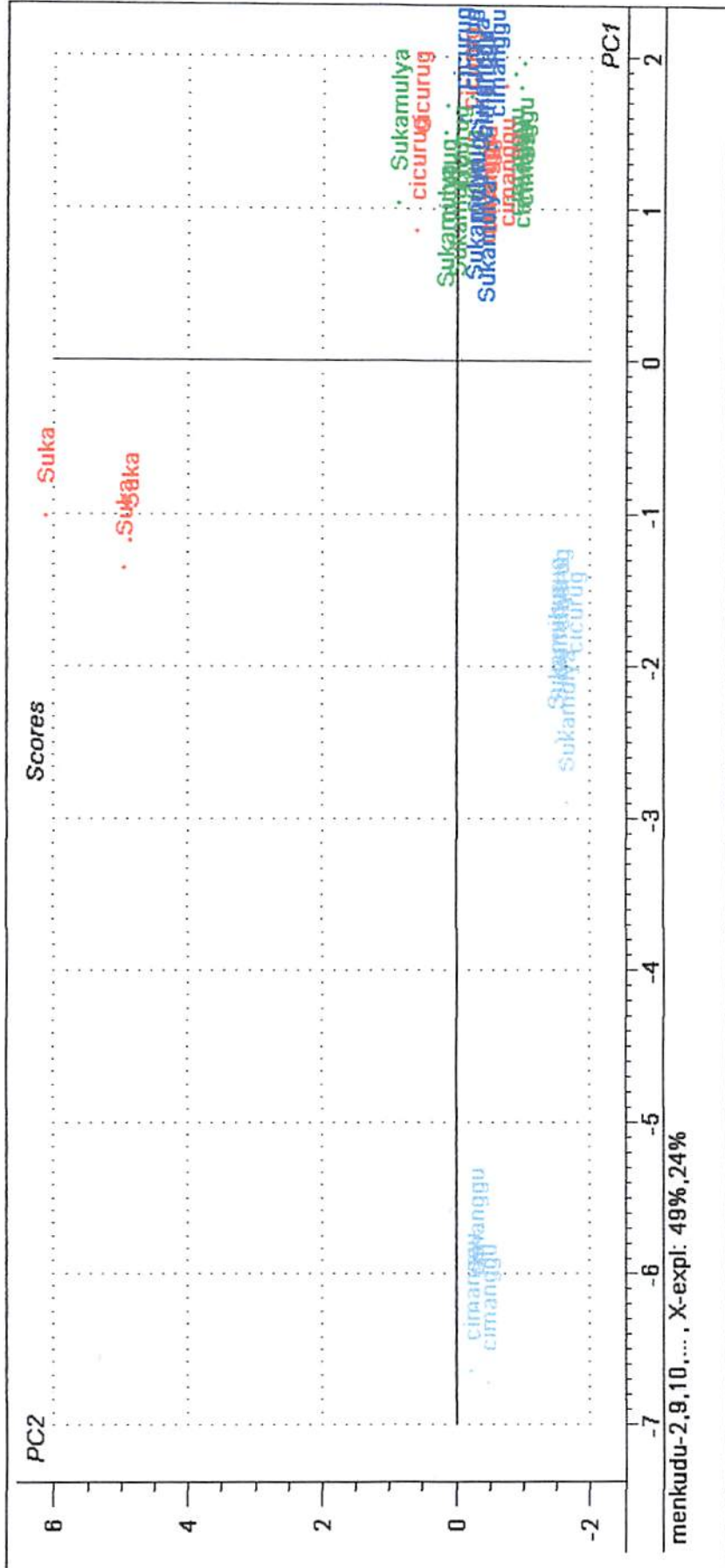
Dengan proses yang sama dilakukan untuk 12 macam ekstrak mengkudu



Gambar 5.3. profil kromatogram dari ekstrak mengkudu

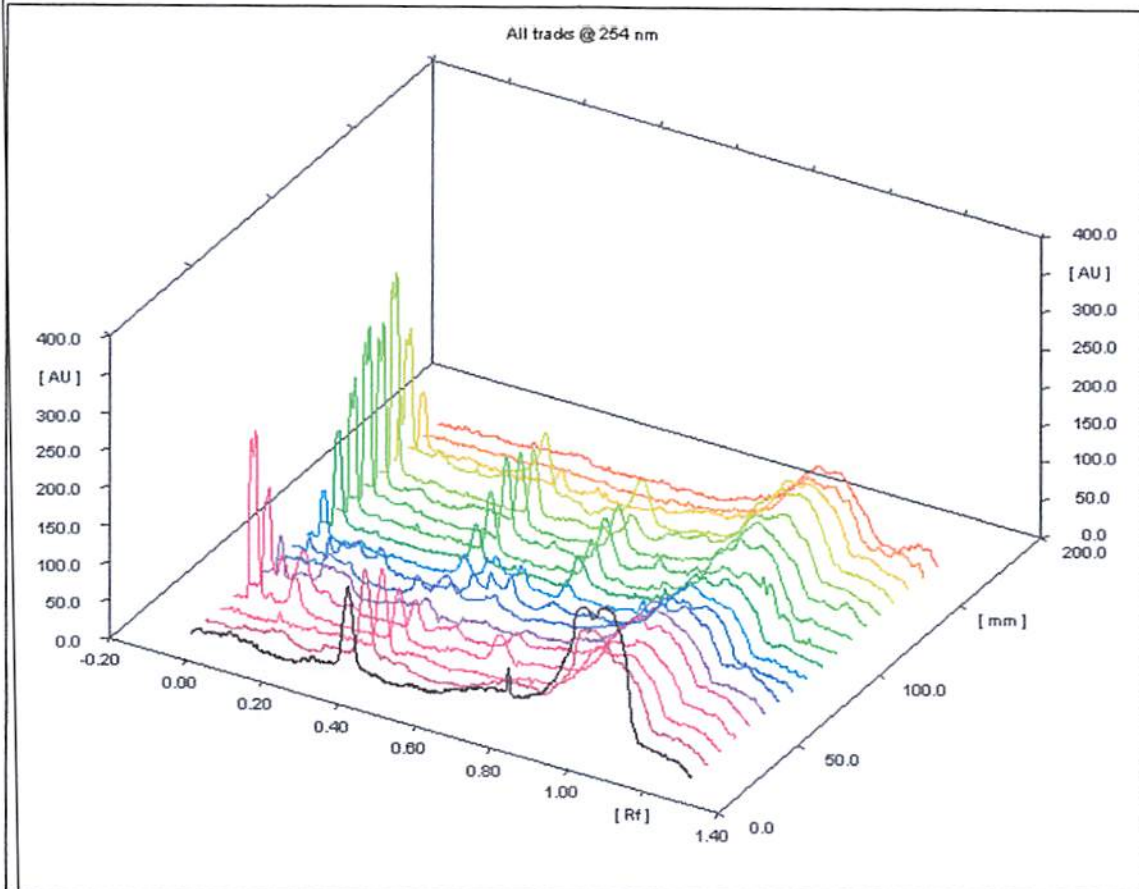
Setelah dilakukan preprosesing data, dilakukan uji statistik dengan menggunakan PCA dan PLS

Hasil uji statistik menggunakan PCA



Gambar 5.4. Score plot ekstrak mengkudu

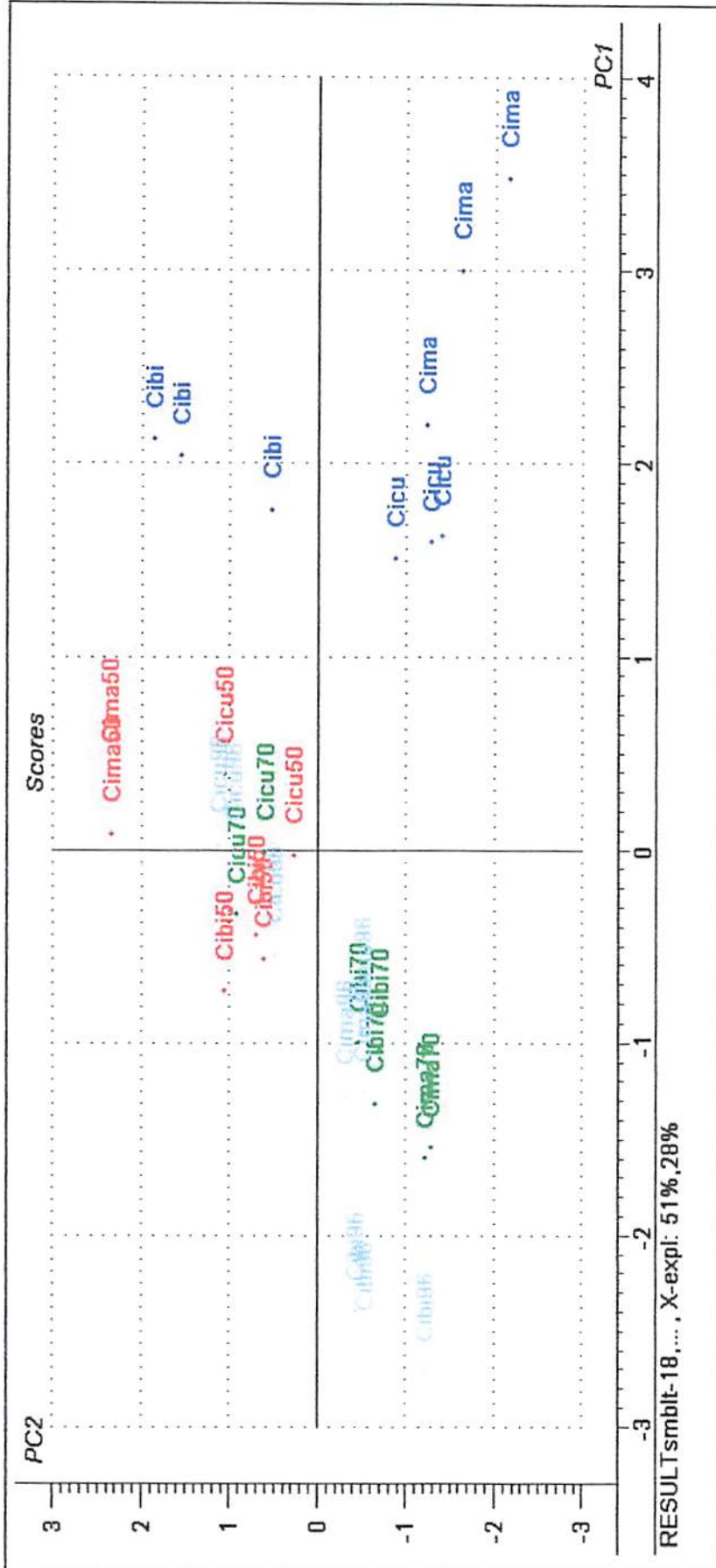
Dengan proses yang sama dilakukan untuk 12 macam ekstrak sambiloto



Gambar 5.5. Profil kromatogram ekstrak sambiloto

Setelah dilakukan preprosesing data, dilakukan uji statistik dengan menggunakan PCA dan PLS

Hasil uji statistik menggunakan PCA adalah sebagai berikut



Gambar 5.6. Score Plot kromatogram ekstrak sambiloto

5.7. Formulasi Fitosom

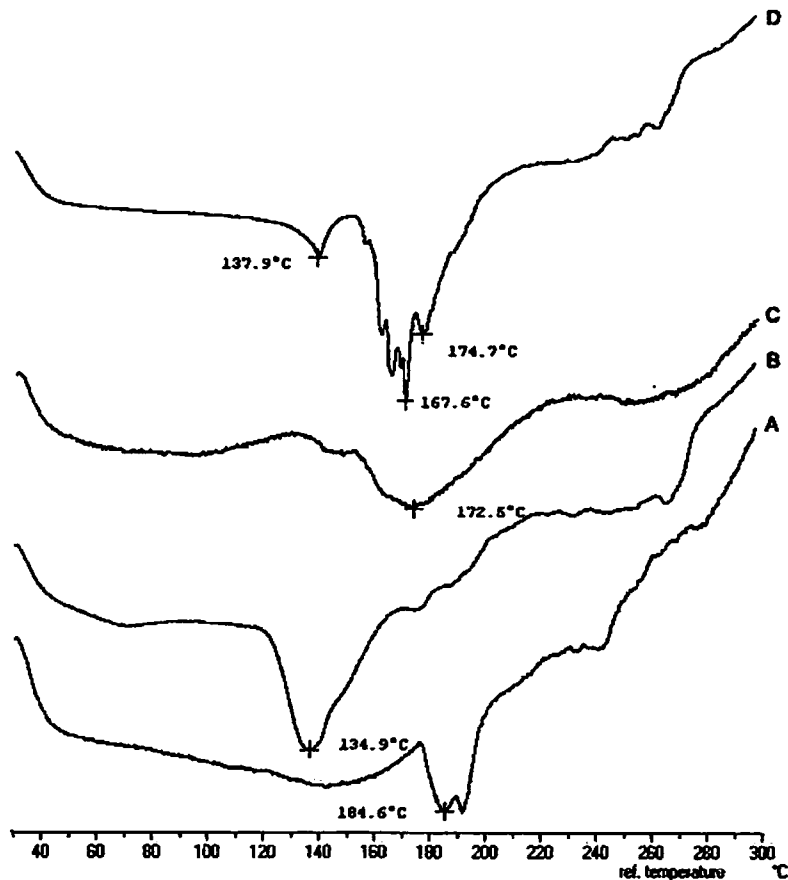
Formulasi fitosom dilakukan untuk meningkatkan/memperbaiki farmakokinetika dari ekstrak, dengan menggunakan suatu bahan, sehingga produk yang dihasilkan akan menjadi lebih baik. Bahan yang digunakan adalah fosfatidilkolin.

Ekstrak ditambah dengan fosfatidilkolin diharapkan bereaksi membentuk suatu yang baru yang mempunyai sifat fisikokimia yang lebih baik bila dibandingkan dengan ekstrak.

Dari hasil karakterisasi hasil formulasi ini diketahui bahwa ekstrak bereaksi dengan baik membentuk sesuatu yang baru sehingga bisa dikatakan bahwa formulasi fitosom ini telah berhasil. Hal ini dapat dilihat pada gambar berikut ini

5.8. Karakterisasi Fitosom dengan DTA(Differential Thermal Analysis)

Teknik analisis menggunakan DTA merupakan teknik yang menarik untuk menggambarkan interaksi antara obat dan excipien dalam suatu formulasi. Apabila dua bahan yang berbeda dibuat kompleks, maka sifat fisika kimianya dapat berubah, misalnya titik lebur, titik didih, atau titik sublimasi bisa bergeser pada temperatur yang berbeda atau bahkan bisa hilang. Hasil penelitian yang telah dilakukan yakni karakterisasi fisik terhadap kompleks ekstrak dengan fosfolipid menggunakan DTA adalah sebagai berikut:

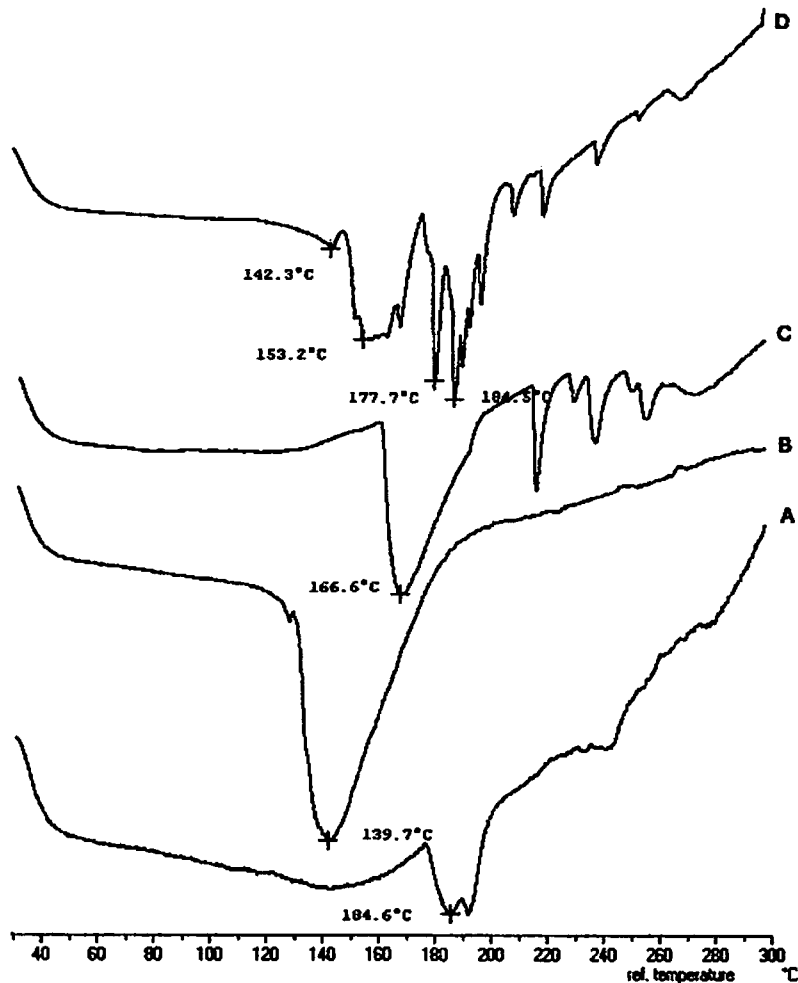


Gambar 5.7. Termogram bahan murni fosfolipid (A) ekstrak sambiloto (B) fitosom sambiloto (C) dan campuran fisik ekstrak-fosfolipid (D)

Gambar 5.7. menunjukkan termogram DTA dari fosfolipid, ekstrak sambiloto, fitosom sambiloto dan campuran fisik ekstrak-fosfolipid. Pada termogram fosfolipid, terlihat dua puncak endotermis yang berbeda tetapi berhimpitan. Puncak endotermis yang pertama terlihat pada 184,6°C dan tidak begitu tajam. Terbentuknya puncak ini dapat disebabkan oleh adanya pergerakan panas dari bagian molekul polar fosfolipid. Tetapi, puncak endotermis yang kedua pada 195°C terlihat lebih tajam, dimana dapat dikatakan bahwa terjadi transisi dari bentuk gel menjadi kristal likuid, rantai karbon-hidrogen pada fosfolipid yang meleleh, berisomer atau adanya perubahan kristal. Sedangkan untuk ekstrak

sendiri, karena bukan merupakan bahan murni, maka termogram yang dihasilkan berupa sebuah puncak endotermis yang melebar dimana titik puncaknya muncul pada 134,9°C. Hal ini juga mengindikasikan adanya molekul air yang hilang dalam jumlah besar, yaitu adanya proses dehidrasi. Campuran fisik dari ekstrak dan fosfolipid dapat dikatakan menunjukkan tiga puncak endotermis yang bisa dibedakan dengan nyata, dimana yang pertama muncul pada 137,9°C (bisa dikatakan sama dengan puncak ekstrak murni); yang kedua pada 167,6°C dan yang ketiga pada 174,7°C (bisa dikatakan sama dengan puncak pertama fosfolipid). Sedikit pergeseran pada puncak-puncak tersebut dapat dijelaskan bahwa apabila temperatur dinaikkan, fosfolipid akan meleleh dan ekstrak akan terlarut dalam fosfolipid dan sebagian dari jumlah tersebut akan membentuk kompleks dengan fosfolipid sesuai dengan teori pada penggunaan metode pelelehan untuk membentuk kompleks. Hasil termogram dari fitosom sambiloto menunjukkan bahwa puncak endotermis ekstrak dan juga fosfolipid menghilang dan temperatur fase transisi menjadi lebih rendah dibandingkan dengan temperatur fase transisi fosfolipid sendiri. Hal ini dapat disimpulkan bahwa ekstrak dan fosfolipid mengalami interaksi-interaksi pembentukan kompleks, seperti adanya transfer muatan antar kedua bahan, atau terjebaknya komponen ekstrak dalam fosfolipid selama proses penguapan solven atau kombinasi keduanya ^[11]. Selain itu juga bisa disebabkan karena adanya interaksi kombinasi dari ikatan hidrogen atau gaya van der Waals ^[12-4]. Terjadinya interaksi antara komponen ekstrak dengan bagian polar dari molekul fosfolipid, menyebabkan rantai karbon-hidrogen pada fosfolipid dapat menjadi bebas dan berikatan kembali dengan bagian polar dari molekul fosfolipid lainnya sehingga sekuens rantai

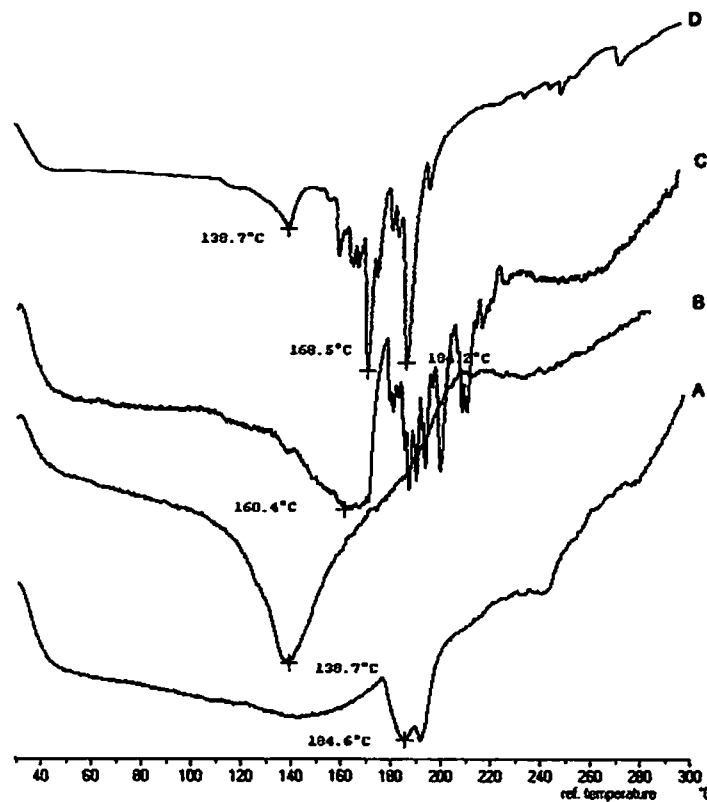
hidrokarbon alifatis menjadi berkurang dan menyebabkan puncak kedua dari fosfolipid juga menghilang dan menekan temperatur fase transisinya sehingga menjadi lebih rendah.



Gambar 5.8. Termogram bahan murni fosfolipid (A) ekstrak pegagan (B) fitosom pegagan (C) dan campuran fisik ekstrak-fosfolipid (D)

Seperti halnya hasil karakterisasi pada ekstrak sambiloto, hasil analisis dengan DTA untuk ekstrak pegagan secara garis besar menunjukkan fenomena yang hampir sama (Gambar 5.8). Termogram dari ekstrak pegagan menunjukkan puncak endotermis yang lebar pada 139,7°C, dimana hal tersebut menunjukkan bahwa selain ekstrak bukan merupakan komponen murni, puncak yang lebar juga

mengindikasikan adanya molekul air yang hilang dalam jumlah besar, yaitu adanya proses dehidrasi. Termogram campuran fisik ekstrak pegagan dan fosfolipid menunjukkan superposisi produk endotermis komponen tunggalnya. Hal ini menunjukkan adanya kehilangan sebagian kristalinitas dan sebagian lagi terjadi kompleksasi dalam matrix fosfolipid. Hasil termogram dari fitosom pegagan, juga menunjukkan hal yang sama pada fitosom sambiloto. Kedua puncak, baik ekstrak maupun fosfolipid menghilang dan terbentuk satu puncak endotermis dengan temperatur fase transisi yang berbeda, yakni pada 166,6°C. Tetapi, selain puncak pada 166,6°C, juga terdapat beberapa puncak endotermis yang muncul pada temperatur tinggi. Hal ini dapat dijelaskan bahwa puncak endotermis yang lebar dan timbul pada 166,6°C disebabkan adanya kehilangan molekul air dari sistem yang terbentuk, kemudian meleleh dengan diikuti oleh terjadinya dekomposisi ekstrak pegagan yang telah kering dan kemudian pelelehan dari komponen hasil dari dekomposisi ekstrak sendiri.



Gambar 5.9. Termogram bahan murni fosfolipid (A) ekstrak mengkudu (B) fitosom mengkudu (C) dan campuran fisik ekstrak-fosfolipid (D)

Hasil analisis DTA dari ekstrak mengkudu (Gambar 5.9), menunjukkan bahwa campuran fisik ekstrak pegagan dan fosfolipid juga menunjukkan superposisi produk endotermis komponen tunggalnya, dimana hal ini menunjukkan adanya kehilangan sebagian kristalinitas dan sebagian lagi terjadi kompleksasi dalam matrix fosfolipid. Masih adanya puncak endotermis pada 138,7°C (i.e. bagian ekstrak) dan 184,6°C (i.e. bagian fosfolipid) menunjukkan bahwa ada bagian ekstrak maupun fosfolipid yang tidak berinteraksi satu dengan yang lain, sedangkan beberapa puncak endotermis pada temperatur tinggi menunjukkan adanya senyawa dekomposisi dari ekstrak akibat peningkatan temperatur yang tidak berinteraksi dengan fosfolipid. Hasil termogram dari fitosom mengkudu, menunjukkan hal yang tidak jauh berbeda dengan campuran

fisiknya. Tetapi jelas terlihat bahwa kedua puncak, baik ekstrak maupun fosfolipid menghilang dan terbentuk satu puncak dengan temperatur fase transisi yang berbeda, yakni pada $160,4^{\circ}\text{C}$. Beberapa puncak yang juga muncul pada temperatur tinggi, dapat dijelaskan seperti halnya yang terjadi pada campuran fisiknya, dimana terjadi kehilangan molekul air dari sistem yang terbentuk, kemudian meleleh dengan diikuti oleh terjadinya dekomposisi ekstrak mengkudu yang telah kering dan pelelehan dari komponen hasil dari dekomposisi ekstrak sendiri. Namun, dapat disimpulkan bahwa pada termogram fitosom mengindikasikan jumlah fosfolipid yang membentuk kompleks dengan ekstrak mengkudu jauh lebih besar dari pada campuran fisiknya.

BAB 6

KESIMPULAN

Dari hasil yang diperoleh dapat disimpulkan sebagai berikut :

1. Berdasarkan kadar senyawa markernya dipilih ekstrak alkohol 50% mengkudu sukamulya, ekstrak alkohol 70% sambiloto Cibinong dan ekstrak alkohol 96% pegagan Manoko
2. Ketiga ekstrak relatif aman untuk digunakan berdasarkan uji toksisitas akut
3. Profil kromatogram ekstrak dapat digunakan untuk kontrol kualitas berdasarkan hasil PCA dan PLS
4. Formula fitosom telah berhasil dengan baik

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Analisis Faktor-Faktor Yang Mempengaruhi Struktur Modal dan Hubungannya Terhadap Nilai Perusahaan

DOES MARKET MICROSTRUCTURE MATTER?: ANALYSIS OF FOREIGN AND DOMESTIC INSTITUTIONAL OWNERSHIP TO AGENCY COST

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Abstract

This research provides measure of absolute and relative equity agency costs for corporations under different ownership and management structures. Our base case is Miller (1977) who proposes a theory explaining the creation of price between selling investor and buying investor. The theory in which Miller proposes loosens the assumption of homogenous expectation in balance model. Miller (1977) argues that divergence of opinion among investors causes the price difference of the price of a security. The dispute mechanism causes the forming price to be further of closer to its intrinsic value. Greater the divergence of opinion, causes greater the gap between the price and its' intrinsic value. This study utilizes Miller's theory which states disputes between buying and selling investor are caused by divergence of opinion, which in this study is focused to the divergence of opinion the magnitude of agency cost. This study tests a new condition that reflects the existence of agency conflict, which is the conditions of stock price premium and stock price discount and related to agency cost control mechanism through foreign and domestic institutional ownership. The two conditions then called as price spread. This study tests four interrelated hypotheses in conditions of stock price premium and stock price discount that are related to agency cost, foreign institutional ownership, and domestic institutional ownership. Analysis method employs complete structural equation model (SEM), and multigroup SEM with constrained and unconstrained parameters. The direction of the study results is found to be consistent with result prediction. Nevertheless, there is one insignificant relationship which is domestic institutional ownership towards agency cost. This indicates that the relationship is practically proven but remains statistically unproven.

Keywords: stock price premium, stock price discount, agency cost, foreign institutional ownership, domestic institutional ownership

Abstrak

Penelitian ini menguji ukuran absolut dan relatif terhadap biaya keagenan pada berbagai kondisi kepemilikan. Penelitian ini berargumen bahwa adanya perbedaan pendapat (divergence of opinion) akan menyebabkan perbedaan harga antara bid dan ask sehingga spread harga saham juga dapat digunakan untuk mengindikasikan adanya biaya keagenan dalam perusahaan. Terdapat dua kondisi yang diuji pada penelitian ini dan merupakan pertamakali diajukan, yaitu kondisi *stock price discount* dan *stock price premium*. Kedua kondisi ini diuji pada perbedaan kepemilikan yaitu kepemilikan asing dan domestik yang juga merupakan mekanisme pengendalian konflik keagenan. Metode analisis statistik yang digunakan adalah SEM dan multigroup SEM. Hasil penelitian menunjukkan konsisten dengan hipotesis bahwa kepemilikan asing mampu menjaga level biaya keagenan yang rendah sedangkan kepemilikan domestik terbukti memberikan hasil statistik tidak signifikan.

Kata kunci: *stock price premium, stock price discount, agency cost, foreign institutional ownership, domestic institutional ownership*

1. Research Background

The social and private costs of an agent's actions due to incomplete alignment of the agent's and owner's interests were brought to attention by the seminal contributions of Jensen and Meckling (1976) on agency costs. Agency theory has also brought the roles of managerial decision rights and various external and internal monitoring and bonding mechanisms to the forefront of theoretical discussions and empirical research. Great strides have been made in demonstrating empirically the role of agency costs in financial decisions such as in explaining the choices of capital structure, maturity structure, dividend policy, and executive compensation. However, the actual measurement of the principal variable of interest, agency costs, in both absolute and relative terms, has lagged behind.

To measure absolute agency costs, a zero agency cost base case must be observed to serve as the reference point of comparison for all other cases of ownership and management structures. In the original Jensen and Meckling agency theory, the zero agency cost base case is, by definition, the firm owned solely by a single owner manager. When management owns less than 100 percent of the firm's equity, shareholders incur agency costs resulting from management's shirking and perquisite consumption. Because of limitations imposed by personal wealth constraints, exchange regulations on the minimum numbers of shareholders, and other considerations, no publicly traded firm is entirely owned by management. Thus, Jensen and Meckling's zero agency cost base case cannot be found among the usual sample of publicly traded firms for which information is readily available. The absence of information about sole owner manager firms explain why agency costs are often inferred but not directly measured in the empirical finance literature.

At one extreme of ownership and management structures are firms whose managers own 100 percent of the firm. These firms, by their definition, have no agency costs. At the other extreme are firms, by their definition, having no agency costs. At the other extreme are firms whose managers are paid employees with no equity in the firm. In the between are firms where the managers own some, but not all, of their firm's equity.

Agency costs emerge when the interests of the firm's managers are not aligned with those of the firm's owners, and take the form of preference for on the job perks, shirking, and making self interested and entrenched decisions that reduce shareholder wealth. The magnitude of these costs is limited by how well the owners and delegated third parties, such as banks, monitor the actions of the outside managers.

Miller (1977) proposes a theory explaining the creation of price between selling investor and buying investor. The theory in which Miller propose loosens the assumption of homogenous expectation in balance model. Miller (1977) argues that divergence of opinion among investors causes the price difference of the price of a security. The dispute mechanism causes the forming price to be further of closer to its intrinsic value. Greater the divergence of opinion, causes greater the gap between the price and its' intrinsic value.

This study utilizes Miller's theory which states disputes between buying and selling investor are caused by divergence of opinion, which in this study is focused to the divergence of opinion the magnitude of agency cost. Divergence of opinion on the magnitude of agency cost in a period will certainly find a dominant party. This is shown by the formation of a closing price which is agreed by buying investor and selling investor.

How does the trade activity reflect a company's agency cost? Stockholders as owners of a company have strong interest with the price of the stocks they own. Beside stockholders, other parties are also interested in the stock price are potential stockholders

or potential investors. The selling and buying process of stocks becomes the process of accomplishment of the agreement point, which produces closing price. How is the process of reaching closing price? Sellers (old stockholders) will sell with an as high ask or offer price as possible and the buyer (potential stockholder or potential investor) will try to buy with as low bid price as possible. In the ending session of ask-bid, closing price will be produced from the price bargaining process between the seller and the buyer.

The next question is how do sellers set an offer price. How do buyers set a bid price? This study proposes an idea that the setting of offer price and bid price reflects conflict of interest between the parties in the company (management, stockholders, and creditors). Conflict of interest between the parties in a company is called agency conflict. Agency conflict, according to Jensen and Meckling (1976), is reflected in agency cost that the company bears and influence the wealth of all stakeholders. If the agency conflict is low, then closing price achieved in the transaction process will be closer to offer price. In the contrary, if the agency cost is high, then closing price achieved in the transaction process will be closer to ask price.

Studies about agency theory ignore the existence of agency conflict that is reflected in the process of achieving closing price through negotiations between offer price and bid price. The studies are more focused on the agency conflict control mechanism. This study tests a new condition, which reflects the existence of agency costs which are stock price premium condition and stock price discount condition and related to agency conflict control mechanism through foreign institutional ownership and domestic institutional ownership. Both conditions are then called price spread. Stock price premium is a condition that shows that closing price of company's closing price tends to be closer to offer price. Meanwhile, stock price discount is a condition that shows that closing price of company's stocks tends to be closer to bid price. Stock price premium and stock price discount show expectations of stockholders for ownership structure and agency cost which effects company's performance. This study proposes that price stock price premium condition and stock price discount are important issue in identifying the agency cost the company has to bear. Both conditions also reflect the level of agency conflict in the company. This study argues that in stock price premium condition, agency conflict is low and agency conflict is high in stock price discount condition.

Closing price of the company's stock that is close to offer price shows that old stockholders (sellers) can obtain a price close to their offer price. Potential stockholders (buyers) are willing to buy with a price close to offer price is possibly because the stock is considered profitable in the future. Old stockholder tend to hold their company's value on to the offer price. If old stockholders are convinced that the value of the company can be increased then they will retain the stock price in high offer price. This causes closing price that is agreed between the parties to be close to offer price. In this case, potential stockholders are also convinced that the value of the company can be increased in the future. This study assumes that an expectation towards high company value is caused by low agency cost. If old stockholders and potential stockholders percept that agency conflict is low, they value the company higher than the value of other similar companies. Closing price condition that is close to offer price in this study is called as stock price premium condition.

Stock price discount condition is a condition in the contrary of stock price premium condition. Closing price that is close to bid price shows that old stockholders (sellers) are forced to sell their stocks with lower price then their offer. This is possibly because the offer price is not responded by the market and old stockholder is in the position to sell their stocks immediately. Potential stockholders (buyers), in this condition, obtain the stocks with a price close to their bid price. In this condition, old stockholders realize that

agency cost of the company is high, thus estimated that the future movement of stock price is unprofitable. Old stockholders are forced to give a discount to potential stockholders. This condition causes the tendency of company's closing price agreed by both parties to be close to bid price. Potential stockholders (buyers) are convinced that high agency cost causes the company's value to be low but the value of the company can still be increased through the mechanism of ownership structure and financial policies of other companies.

This study conducts observations of information of daily closing price (agreed) between sellers and buyers and the difference between offer price and closing price, and between bid price and closing price. Therefore, we can say that this study employs the perspective of market microstructure to explain agency cost. Studies in the subject of microstructure give a deep understanding in examining the behavior and operation of the capital market based on intra-day movement. This study employs a microstructure approach that is combined with corporate finance research model.

Amihud and Mendelson (1986) states that bid ask spread measurement can be used to determine price of an asset (stocks, bonds, and others). Their studies in the microstructure are also useful to determine the value of an asset in corporate finance. This study relates the findings of bid-ask spread as an indicator in determining stock price with agency cost and introduce price spread condition, which consists of stock price premium and stock price discount.

So far, studies on the agency theory do not test the existence of bargaining between old stockholders (sellers) with potential stockholders (buyers) in achieving closing price. Different closing prices reflect different agency conflicts among companies. The effect of different agency conflicts among companies will cause a number of companies to be in stock price premium condition and others in stock price discount condition. The condition of stock price premium and stock price discount difference causes the effect of foreign institutional ownership and domestic institutional ownership as agency conflict control mechanisms towards agency cost to be different. Identification of stock price premium and stock price discount conditions in this study is expected to give better explanation the different effects various agency cost reduction mechanism. This study focuses on foreign institutional ownership and domestic institutional ownership as agency conflict reduction mechanism.

The existence of different results from past studies about the relationship between foreign institutional ownership and domestic institutional ownership to agency cost urge researcher to test their relationship between the three constructs. This study also introduces price spread condition, which is expected to explain the difference among the effects of agency conflict control mechanism through foreign institutional ownership and domestic institutional ownership better.

2. Literature Review and Hypothesis Development

2.1. Agency Cost

The core of agency theory is the existence of conflict of interest between agents and principal. The agency cost, which occurs because of this conflict of interest, reduces the value of the company. Equity agency cost includes monitoring cost, bonding cost, and residual loss (Jensen and Meckling, 1976). Monitoring cost include principals' expense, in the effort to control agent's behavior through budget tightening, compensation policy, and operational regulations. Bonding costs are the agent's expense to guarantee that agents will not conduct certain actions that will inflict financial loss towards principals or to guarantee that principals will give compensations if agents conduct certain actions.

Residual loss includes the monetary value of principals' wealth reduction because of different interests between agents and principals, which stimulate agents, conduct selfish actions and inflict financial loss to principals. The action of this agent can be in the form of inefficient actions such as investing in unprofitable investments or make wasteful expenses. Moreover, there is also debt agency cost that includes paying too much dividend, monitoring cost, and bonding cost. Reduction of agency cost can be achieved through a number of mechanisms such as through manager stock ownership, combining financing sources from debts and equities, and dividend payout (Crutchley and Hansen, 1989).

This study will relate agency cost and price spread condition between stock price premium and stock price discount experienced by the company. Agency conflict experienced by the company will be reflected in the spread of stock price premium and stock price discount of the company. Agency conflict reflected in the stock price premium and stock price discount condition are an agency conflict that is called perceived conflict. Therefore, this study employs perceived agency conflict (stock price premium and stock price discount) to explain actual agency conflicts.

2.2. Price Spread: Stock Price Premium and Stock Price Discount

Baker and Wurgler (2004a, 2004b) employ the term stock price premium to explain reasons of companies that pay dividend and companies that do not pay dividend. This study adopts the term stock price premium and stock price discount but to test the influence of ownership structure and agency cost towards company performance. Stock price premium and stock price discount will be called price spread condition.

Price spread condition of stock price premium and price spread conditions of stock price discount are implications from company's agency conflict. Closing price that is close to offer price and bid price shows that buyers and sellers do take into account agency cost in daily transactions. The level of agency conflict will cause difference between closing price and the offer and bid price. The stock price premium condition shows that the closing price of a company is close to offer price. The stock price premium condition reflects the low level of agency conflict. On the other hand, the stock price discount condition shows that the closing price of a company is close to bid price. The stock price discount condition reflects the low level of agency conflict.

2.3. Foreign Institutional Ownership and Domestic Institutional Ownership

Ownership structure becomes important in agency theory because most agency conflict arguments are caused by ownership and control separation. Agency conflict does not occur in companies with 100% management ownership (Jensen and Meckling, 1976). The condition where new owners buy company's stocks causes discrepancy of interest between the parties in the company. Pure conflict occurs between principals and agents as discussed in positivist agency theory and conflicts between stockholders, management, employees and other parties are within principal-agent research (Eisenhardt, 1989).

Institutional ownership can be used to reduce agency conflict (Shleifer and Vishny, 1986; Jarrel and Poulsen, 1987; Brickley, Lease and Smith, 1988; Graves and Waddock, 1990; Han, Lee and Suk, 1999; and Varma, 2001). The studies argue that a company will be monitored better by institutions that invest in the company. Institutions have professionals in the field of investing which understands the appraisal mechanisms of companies and conduct monitoring towards managers.

Institutional ownership selling will drive down the price of the stocks therefore institutional owners avoid selling their stocks and they conduct monitoring towards the company instead. Institutional ownership expects by conducting effective monitoring the

value of the company would increase. The most efficient method employed by institutional owners is by informal discussions with managers.

Hypothesis development is based on the argument that this study is developed in the conceptual element. Hypothesis development sub chapter in this study consists of a number of components which are foreign institutional ownership, domestic institutional ownership, agency cost, and company performance in stock price premium and stock price discount condition.

Agency theory argues that institutional ownership will decrease agency conflict because the institution will help monitor the company so management will not conduct actions that will inflict financial losses towards stockholders (Crutchley, Jensen, Jahera, and Raymond, 1999; Chen and Steiner, 1999). This is valid in the condition where institutional owner partially monitor the management. However, in the condition where institutional owner is the majority owner, then monitoring would be focused only for the interest of owning institution and ignores public stockholders interest. Foreign institutional ownership can be utilized as control method to decrease agency cost. The higher the foreign institutional ownership, the lower the agency cost and the lower the foreign institutional ownership, the higher the agency cost. Therefore, hypothesis H₁ is as follows:

H₁: Foreign institutional ownership has negative influence towards agency cost

This study assumes that agency conflict in stock price premium condition will be lower compared to stock price discount condition. This assumption cause's agency conflict reduction mechanism through foreign institutional ownership in stock price premium condition will have influence less negative compare to stock price discount condition. Companies with low agency conflict will closely observe the cost to control agency conflict. So they tend to decrease conflict reduction mechanism through ownership structure to drive cost down. Therefore, hypothesis H₂ is as follows:

H₂: Foreign institutional ownership will affect agency cost negatively; lower when firm is in stock price premium than stock price discount condition

Domestic institutional ownership also acts as a monitoring party, similar to foreign institutional ownership. Core and Larcker (2002) found a negative relationship between stock performance and domestic institutional ownership. Companies with high institutional ownership (more than 5%) indicate its ability to monitor the management. Great institutional ownership causes the utilization of company's assets to be more efficient. Therefore, the proportion of institutional ownership acts as a method to prohibit management from inefficient.

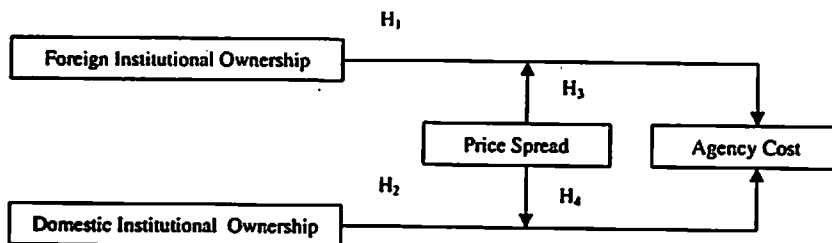
Ismiyanti and Hanafi (2004) found that the average institutional ownership in 1997-2001 period reaches 66% of total stocks outstanding. This result shows that 34% of stocks are held by public (individual) investors, management, directors, and institutional ownership. This is different in the United States, institutional ownership reaches 52,36% from total stocks outstanding in 1999 (Chen and Steiner, 1999). Domestic institutional ownership can be utilized as control method to decrease agency cost. Therefore, hypothesis H₃ is as follows:

H₃: Domestic institutional ownership has negative influence toward agency cost

This study assumes that agency conflict in stock price premium condition will be lower compared to stock price discount condition. This assumption cause's agency conflict reduction mechanism through foreign institutional ownership in stock price premium condition will have influence less negative compared to stock price discount condition. Companies with low agency conflict will closely observe the cost to control agency conflict. So they tend to decrease conflict reduction mechanism through ownership structure to drive cost down. Therefore, hypothesis H_4 is as follows:

H_4 : Domestic institutional ownership will affect agency cost negatively; lower when firm is in stock price premium than stock price discount condition

The relationship between foreign institutional ownership, domestic institutional ownership and agency cost through stock price premium and stock price discount condition, describes in research framework Figure 1 below:



Note: Price spread consists of stock price premium and stock price discount

Figure 1. Research Framework

3. Research Methods

3.1. Sample and Data

Samples employed in this study are non-financial companies listed in Jakarta Stock Exchange from 1995 to 2004. Financial data obtained from annual financial report which consists of balance sheet, income (profit and loss) statement, cash flow report, and financial report notes. The data source for the study is Jakarta Stock Exchange Library, Indonesian Capital Market Directory (ICMD), and Indonesian Securities Market Database (ISMD) published by Faculty of Economics Gadjah Mada University.

3.2. Variables

Agency cost proxy employed in this study refer to asset utilization and operational cost (Ang, Cole, and Lin, 2000); and free cash flow (Hackel, Livnat, and Rai, 1996) but with adaptation based on certain benchmark value. Agency cost calculation method ideally uses the difference of residual loss from 100% company ownership minus residual loss from non 100% ownership. Sample collection constraint towards 100% company ownership causes the utilization of a benchmark value. The asset utilization measure agency cost based on asset turnover. Asset turnover is a ratio between total sales and total asset. Selling and General Administrative (SGA) is included in operational expense proxy.

Operational expense measures the agency expenses based on SGA which a ratio between operational expense and total sales. Free cash flow used in this study employs free cash flow counting method developed by Hackel, Livnat, and Rai (1996) which modifies the traditional free cash flow calculation. This method was selected because it is the most appropriate method for the condition of cash flow statement in Indonesia to avoid sample decrease.

$FCF = TFCF + DOCO + DCEX$
 $TFCF = (OCR - OCO) - CEX$
 TFCF = traditional free cash flow
 OCR = operating cash inflow
 OCO = operating cash outflow

CEX = capital expenditure
 $DOCO = (OCOGrowth - salesgrowth) * 2,0 (* OCO)$
 DOCO = discretionary operating cash outlay; Hackel, Livnat, and Rai (1996) assumes 20% of OCO is discretionary of OCO and sales growth.

$DCEX = (CEXgrowth - CostofGoodsSoldGrowth *) CEX$
 $DCEX = \text{discretionary capital expenditure } OCO \text{ growth} = (OCO_t - OCO_{t-1}) / OCO_{t-1}$
 $Sales \text{ Growth} = (Sales_t - Sales_{t-1}) / Sales_{t-1}$
 $CEX \text{ growth} = (CEX_t - CEX_{t-1}) / CEX_{t-1}$
 $Cost \text{ of Goods Sold (COGS) Growth} = (COGS_t - COGS_{t-1}) / COGS_{t-1}$

Stock price premium show that closing price tends to be close to offer price. Stock price discount show that closing price tends to be close at bid price.

$Stock \text{ Price Premium} = |Closing \text{ Price} - Offer \text{ Price}|$
 $Stock \text{ Price Discount} = |Closing \text{ Price} - Bid \text{ Price}|$

Foreign institutional ownership is the sum and percentage of stocks owned by foreign institution. Domestic institutional ownership is percentage ownership by a legal entity registered as non-public stockholder.

3.3. Method of Analysis

This research employs Structural Equation Modeling (SEM) in hypotheses testing because SEM has the ability to combine measurement model and structural model. This research applied two stage approaches for multigroup structural equation modeling (MSEM). MSEM do not require nested model to estimate different hypotheses groups in path-analytic model coefficient or model fit coefficient. A series of statistical goodness-of-fit indicators were employed to test a complex model for every group.

Moderating variable test is SEM was conducted in two structural models, which are constrained parameters model and unconstrained parameters model. In models with constrained parameters, regression estimate weight is controlled for both sample groups thus having similar estimated relationship. Moderating variable is significant if models with unconstrained parameters are better than models with constrained parameters.

4. Result and Discussion

Result of full structural equation model in this research will be used to analyze research hypotheses that do not contain stock price premium and stock price discount moderating variables, which are H₁ and H₃ (Table 1). Hypotheses which used stock price premium and stock price discount moderating variables (H₂ and H₄) are tested by employing multigroup structural equation model by using constrained parameters and unconstrained parameters models.

Table 1. Result of Full Structural Equation Model

Structural Relationship		Unstandardized Regression Weight	Standard Error	Critical Ratio
Agency Cost	Foreign Inst. Ownr.	-0.243	0.086	-3.481*
Agency Cost	Domestic Inst. Ownr.	-0.378	0.092	-0.643
Asset Utilization	Agency Cost	1.000		
Operating Expense	Agency Cost	0.863	0.078	5.429*
Free Cash Flow	Agency Cost	0.068	0.089	0.983

Table 2 shows test result by multigroup structural equation model with constrained parameters. Regression coefficient value of ownership structure influence (foreign institutional ownership and domestic institutional ownership) towards agency costs is not different when compared between stock price premium sample and stock price discount sample. The numbers of data used for the study are 1559 samples comprising of 713 samples with stock price premium and 846 samples in stock price discount.

Table 2. Result of Price Spread Multigroup Structural Equation Model with Constrained Parameters

Structural Relationship	Stock Price Premium Sample		Stock Price Discount Sample	
	Unstandardized Regression Weight	Critical Ratio	Unstandardized Regression Weight	Critical Ratio
AC PFIOWN	-0.483	-7.195*	-0.483	-7.195*
AC PDIOWN	-0.036	-0.457	-0.036	-0.457
AU AC	1.000		1.000	
OE AC	0.079	3.159*	0.079	3.159*
FCF AC	0.275	2.064	0.275	2.064
Goodness of Fit				
Chi Square	259.652		GFI	0.942
Degree of Freedom	57		AGFI	0.931
Probability	0.000		RMR	0.006
Chi Square/DF	4.555		RMSEA	0.062

Table 3 shows test result by multigroup structural equation model with unconstrained parameters. Regression coefficient value of ownership structure influence (Foreign institutional ownership and domestic institutional ownership) towards agency cost is not different when compared between stock price premium sample and stock price discount sample. The numbers of data used for the study are 1559 samples comprising of 713 samples with stock price premium and 846 samples in stock price discount.

Goodness of fit of model with unconstrained parameters (GFI= 0.976) is found to be better than model goodness of fit of model with constrained parameters (GFI= 0.942). In addition, the difference at chi square value is 56.585 with 4 degree of freedom show a significant result ($p < 0.10$). Therefore, base model and alternative model based on the difference of stock price premium and stock price discount are significantly different. This indicates that different price spread condition significantly influential as moderating variables. Variable moderation of price spread condition is mainly seen on the difference between foreign institutional ownership, domestic institutional ownership, and agency cost on stock price premium and stock price discount. Comparison between base model and alternative model is shown in Table 4.

Table 3. Result of Price Spread Multigroup Structural Equation Model with Unconstrained Parameters

Structural Relationship	Stock Price Premium Sample		Stock Price Discount Sample	
	Unstandardized Regression Weight	Critical Ratio	Unstandardized Regression Weight	Critical Ratio
AC PFIOWN	-0.542	-3.267*	-0.946	-6.465*
AC PDIOWN	-0.087	-0.785	-0.236	-1.463
AU AC	1.000		1.000	
OE AC	0.085	5.078*	0.098	4.842*
FCF AC	0.497	3.287*	0.096	0.823
Goodness of Fit				
Chi Square	203.067		GFI	0.976
Degree of Freedom	53		AGFI	0.943
Probability	0.000		RMR	0.028
Chi Square/DF	3.831		RMSEA	0.067

Table 4 shows comparison of test result between base model (constrained model) and alternative model (unconstrained model). The values being compared are goodness of fit value, chi square value, and degree of freedom of both test models to determine whether stock price premium and stock price discount is significantly moderate relationships in this model. Table 4 shows the result of test comparison using constrained parameters and unconstrained parameters. The table shows increase of goodness of fit values, from base model to alternative model. Goodness of fit value analyzed is chi square value which changed 56.585 points and degree of freedom which changed 4 points. Based on goodness of fit of base model and alternative model, it can be concluded that relationship between variable of agency cost and performance, moderated by stock price premium and stock price discount.

Table 4. Comparison of Goodness of Fit from Base Model and Alternative Model of Price Spread

Indicator	Goodness of Fit		Criteria
	Base Model (constrained parameter)	Alternative Model (unconstrained parameter)	
Chi Square	259.642	203.067	Low
Degree of Freedom	57	53	
Probability	0.000	0.000	> 0.05
Chi Square/DF	4.555	3.831	< 5
GFI	0.942	0.976	> 0.90
AGFI	0.931	0.943	> 0.90
RMR	0.006	0.028	< 0.03
RMSEA	0.062	0.067	< 0.08
Goodness of Fit Increase from Base Model to Alternative			
Chi Square	259.652-203.067 = 56.585		High
Degree of Freedom	57 - 53 = 4		
Probability	Less than 0.005		< 0.05
Conclusion	Alternative model is significantly different from base model. Thus, price spread (stock price premium and stock price discount) significantly moderates direct and indirect relationship between ownership structure and agency cost		

Table 5 is a summary table between result predictions with research results which utilizes full structural equation model with constrained parameters and unconstrained parameters model in stock price premium and stock price discount as moderating variable. Table 6 shows comparison result prediction with model test result using full structural equation model. The direction of the study results are found to be consistent with result prediction which are negative. Nevertheless, there is one insignificant

relationship which is domestic institutional ownership towards agency cost. This indicates that the relationship is practically proven but remain statistically unproven.

Table 5. Comparison of Test Result Prediction with Unmoderated Full Structural Equation Model

Relationship	Result Prediction	Full SEM Result
Agency Cost \leftarrow Foreign Institutional Ownership	Negative	- 0.243*
Agency Cost \leftarrow Domestic Institutional Ownership	Negative	- 0.378

Table 6 is a summary table between result predictions with research results which utilizes multi-group structural equation model in stock price premium and stock price discount as moderating variable. The result of the study shows that coefficient value of stock price discount should be lower than coefficient value of stock price premium. The influence of agency cost towards performance is found to be different. Coefficient of stock price premium is lower than stock price discount.

Table 6. Comparison of Test Result Prediction with Multi-group Structural Equation Model Moderated by Price Spread

Relationship	Result Prediction	Test Result Prediction With Multigroup Structural Equation Model Moderated by Price Spread	
		Stock Price Premium	Stock Price Discount
Agency Cost Foreign Inst. Ownership	SPD<SPP<0	-0.542*	-0.946*
Agency Cost Domestic Inst. Ownership	SPD<SPP<0	-0.087	-0.236

5. Result and Discussion

Table 7 show a summary of hypotheses test result of the study. The table is the test result of this study.

Table 7. Summary of Hypothesis Test Result of the Study

Hypothesis	Test Result
Structural equation model on all study samples	
H ₁ : Foreign institutional ownership have negative influence towards agency cost	◆◆
H ₃ : Domestic institutional ownership have negative influence towards agency cost	◆
Structural equation model on stock price premium and stock price discount samples	
H ₂ : Foreign institutional ownership will affect agency cost negatively; lower when firm is in stock price premium than stock price discount condition.	◆◆
H ₄ : Domestic institutional ownership will affect agency cost negatively; lower when firm is in stock price premium than stock price discount condition.	◆

Explanation:

◆◆: Empirical result consistent to theoretical prediction and significant

◆: Empirical result consistent to theoretical prediction and not significant

Next studies are expected to reexamine agency conflict magnitude proxy through stock price premium and stock price discount. This is to support the findings of this study and that the proxy is able to be used as measurement method of agency conflict in Indonesia. Further studies can also develop other mechanisms in agency conflict control such as debt policy and dividend policy. This will enrich findings that support measurements of stock price premium and stock price discount conflict. For investors, this study suggests investors to select companies which have low agency conflicts. This will then influence the company's stock prices. Companies will then be encouraged to reduce conflict and increase their financial performance. If this situation can be achieved Indonesia will be a profitable investment area.

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IKATAN AKUNTAN INDONESIA
KOMPARTEMEN AKUNTAN PENDIDIK



Does Debt Affect Firm Financial Performance? The Role of Debt on Corporate Governance in Indonesia

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This research addresses main question of the conditions of debt-constraint expropriation and debt-facilitate expropriation, and the difference between those conditions on type of group ownership (group or no group-affiliate). Agency theory predicts that debt is bonding and monitoring mechanism for managers' perquisites action. Expropriation of minority shareholders by majority shareholders hurts good corporate governance practices. The expropriation also hurts debtholders value. The research argues that the use of debt will minimize the expropriation level and maintain certain control to managers and majority shareholders, on behalf of minority shareholders and debtholders. The problem of majority versus minority and debtholders spreads widely in Indonesia. This research conducts analytical and statistical methods to examine the roles of debt policy as mechanism of good corporate governance practices in Indonesia. This research argues that debt has difference effect on financial performance based on certain debt characteristic. Two characteristics of debt are debt-constraint expropriation (DCE) and debt-facilitate expropriation (DFE). Different types of ownership, which are group and no group-affiliate, are also examined to support the main issues of DCE and DFE. The result will be useful for economic policy makers; firms level policy makers, investors, academicians, and researchers in the area of finance, social science, and humanities. The research tests the main question with four hypotheses using ordinary least squares (OLS) regression and Wald test for coefficient test. The result shows support for differences in effect on debt to performance for DCE (positive effect) and DFE (negative effect). On DCE, no group-affiliate firms have higher positive effect of debt on performance than group-affiliate firms do. However, on DFE due to risk reduction mechanism, group-affiliate firms have less negative effect of debt on performance than no group-affiliate firms do.

Keywords : constraint, facilitate, debt, performance, agency, group.

1. Introduction

The role of debt in corporate governance depends on how governance is exercised, i.e., on the structure of corporate ownership and control. Default on corporate debt might not affect the professional manager's net worth, but would certainly devastate his reputation and career. This would not be a concern for the controlling shareholder of a corporate group, who employs himself or herself as top manager and can borrow through a group affiliate from a group bank. Consequently, debt could constraint the expropriation of dispersed shareholders by professional managers, as in the U.S., yet it could facilitate the expropriation of minority shareholders by the controlling shareholders of the corporate groups that dominate the business scene in Indonesia.

This research is considering the ownership, control and debt of all listed corporations with credible accounting data of the firms listed in Indonesia. This research argues that capital market in Indonesia is ineffective and more vulnerable to expropriation as well as more levered. The condition is giving the controlling shareholder more expropriations of the resources without direct control from debtholders.

Indonesian firms have a controlling block of shares held by major shareholder. The condition supports the argument that the key agency problem is between the controlling (majority) and minority shareholders. The controlling shareholder often exerts control through a pyramid structure. Controlling shareholders have control rights in firms in excess of their control right, and they also participate in management (La Porta, Silanes, and Shleifer, 1999). Wolfenzon (1998) argues that pyramids should be also more common in countries with poor shareholders protection. Mahadwartha (2004) tested the entrenchment and alignment hypothesis for internal institutional ownership¹ in Indonesia and found that alignment mechanism is higher for high internal institutional ownership firm.

In their pioneering analysis of the agency problem between professional managers and dispersed shareholders, Jensen and Meckling (1976) argued that debt constrains managerial expropriation by imposing fixed obligations on corporate cash flow. Jensen (1986, and 1989) further examined this argument in the context of free cash flow, debt, and leveraged buyouts. Jensen argues that free cash flow, debt, and leverage buyout forced managers to disgorge their corporations' free cash flow, replacing equity with debt.²

¹ Internal institutional ownership is term introduced by Mahadwartha (2004) to describe the uniqueness of ownership in Indonesia. Internal institutional ownership is ownership held by regular business institution, and not by financial firms.

² Easterbrook (1984) argues that debt forces managers to be accountable to the external capital market. Lang et al (1996) document that debt curtails investment by firms with poor prospects, and that leverage increases when growth opportunities are less (see also Kim and Sorenson (1986), Titman and Wessels (1988)). Maloney et al (1993) document that leverage improves managerial decision making on key issues like acquisitions.

Other constraint for debt to impose on managerial expropriation in the U.S. is the role of managers' reputation in the labor market (Fama and Jensen, 1983a, 1983b). Although the manager is not personally liable for his corporation's debts, default would trigger winding-up proceedings that would force him to search for re-employment, just when his reputation had been crippled. However, debt could play a different role in corporate governance if managers whose reputation and career are not tied specifically to the corporation liable for the leverage made the key decisions.

In contrast to the US firms, Indonesian firms have a controlling block of shares held by major shareholder. The condition supports the argument that the key agency problem is between the controlling (majority) and minority shareholders. The controlling shareholder often exerts control through a pyramid structure. Controlling shareholders have control rights in firms in excess of their control right, and they also participate in management (La Porta, Silanes, and Shleifer, 1999).

Wolfenzon (1998) argues that pyramids should be also more common in countries with poor shareholders protection. Mahadwartha (2004) argued that firm with high internal institution will better control for managers perquisites and hopefully protect debtholders interest. However, the main question focuses on the interest of majority shareholders and minority shareholders. Internal institutional ownership is usually representation of majority shareholders or founder shareholders.

To illustrate the expropriation, this research shows as follows: If the controlling shareholder owns 100% of corporation X, which owns 60% of corporation Y, which owns 25% of corporation Z, then its ownership rights (O) in Z are $O = 100\% \times 60\% \times 25\% = 15\%$, yet, through its majority control (C) of X and Y, its control rights in Z are $C = 25\%$, usually enough for effective control. By directing Z to buy goods or assets from X at a premium, the controlling shareholder expropriates 100% - 15% of the premium from Z's other shareholders.

Claessens, Djankov, and Lang 1999a, and 1999b; and La Porta, Silanes, Shleifer, and Vishny, 2000 introduced the measurement of an affiliate's vulnerability to such an expropriation by the ratio O/C. The O/C ratio is controlling shareholder's ownership rights O (defined as its percentage claim on the affiliate's cash flows) to its control rights C (calculated by identifying the weakest link in each control chain and linking it to the controlling shareholder, then summing the percentage control rights across these links). A low O/C ratio indicates that the controlling shareholder has the incentive and the ability to use unfairly-priced transactions to shift cash from the affiliation to affiliates higher up the pyramid, in which it has higher ownership rights.

Within a corporate pyramid, increase indebtedness by an affiliate needs not constraint expropriation by the controlling shareholder because the leverage can be rolled over by group banks, recycled into external loans guaranteed by other affiliates, or reshuffled ahead of auditors to other affiliates by intra-group loans or transfer pricing. Even a default by the affiliate needs not damage the reputation of the manager/controlling shareholder if the affiliation is an obscure control webs passing through several layers of the pyramid.

In any case, a manager can shrug off reputation of controlling shareholder who employs himself or herself within the pyramid, in contrast to the severe problems that

default would cause a professional manager thrown onto the external manager market tainted by clear responsibility for the defaulting firm. Thus, the higher fixed obligations will not constraint the controlling shareholder more tightly. On the contrary, it could facilitate expropriation of the affiliate by allowing the controlling shareholder to control more resource without diluting his control stake or assuming more liabilities directly.³

Those expropriations can include not only minority shareholders, but also creditors left with uncollectible leverage and tax payers forced to bail out the financial system endangered thereby. This research seeks to distinguish the relationship of debt to firm performance based on the conditions of Debt-Constraint Expropriation (DCE) and Debt-Facilitate Expropriation (DFE), and using the empirical relationships that estimates in each condition of group-affiliate and no group-affiliate firms. Testing the argument requires an assumption that debt on DCE and DFE has different purposes based on firm's interest of using debt. This determines whether debt decisions are dominated by the concerns of informed external suppliers of capital or by the interests of the controlling shareholder.

This research argues that governance mechanisms can reduce default risk by mitigating agency costs and monitoring managerial performance and by reducing information asymmetry between the firm and the lenders. Corporate governance plays a significant role on shareholders, and debtholders protection. Debt as monitoring mechanism on agency conflict (Ismiyanti and Hanafi, 2004) is debtholders representation of interest on firm financial performance. Meanwhile, corporate governance is also concerned with the conflict of majority and minority shareholders, and debt as governance mechanism will reduce the conflict especially on the conditions of debt as constraint expropriation.

Indonesia confirms that capital market institutions are ineffective so that controlling shareholders (i) dominate decisions on debt, at least amongst group-affiliate firm, and (ii) exploit this to increase the debt of firm more vulnerable to expropriation, presumably to acquire more resources to expropriate. Who lends to Indonesia corporations that are more vulnerable to expropriation? Loans could be from "related parties" sharing a controlling shareholder with the borrower. The facts brought the idea to also test the condition of group and no group-affiliate.

1.1. Research Problems and Objectives

As described on the introduction section, this research has several problems to address. The problems include testing debt effect on firm financial performance, and the effect based on debt-constraint and debt-facilitate expropriation, and the issues regarding group and no group-affiliate. Details of research problems are:

³ In a U.S. context, Harris and Raviv (1988) and Stulz (1988) argue that controlling shareholders may use leverage to inflate the voting power of their shares, and reduce the discipline of the market for corporate control. Stulz (1988) shows that managers who value control very highly rely primarily on debt financing in order to minimize dilution of their equity stakes in the firm, thus making the firm less vulnerable to hostile takeover.

- a. Is the effect of debt on firm financial performance positive when debt-constraint expropriation (DCE)?
- b. Is the effect of debt on firm financial performance negative when debt-facilitate expropriation (DFE)?
- c. Is the effect of debt on firm financial performance different between group-affiliate and no group-affiliate, if DCE exist?
- d. Is the effect of debt on firm financial performance different between group-affiliate and no group-affiliate, if DFE exist?

1.2. Research Originals

The arguments and issues in this study are different from previous studies in some points of view. First, previous studies discussing debt as governance mechanism in Indonesian are lack of support on the role of debt as governance mechanism. Ismiyanti and Hanafi (2004); Mahadwartha (2002); and Mahadwartha (2004) focused on the interdependence relationship between financial policies such as debt, dividend, and investment.

This research focuses on several specific conditions that matters on the issues of debt as governance mechanism such as expropriation. Second, while there is a great deal of empirical research on corporate governance, very little of it concerns the behavior of debt as constraint or facilitate expropriation, or the condition that supports such an expropriation. This study attempts to investigate these behaviors in empirical study on Indonesian listed firms.

1.3. Research Contributions

Transparency international published their corruption perception index on 2005, and Indonesia's score is 2.2 (scale of 10). The level of corruptions in Indonesia is very high and in the end will degenerate economic growth. Only Malaysia with score 5.1, and Singapore with 9.4 have better score than other Asian countries. Meanwhile Thailand with 3.8, and Philippines with 2.5 also shows mediocre and high corruption level.

This research will help government, investors and regulators to examine in scientific approach the corporate governance implementation as tools to control firm's level corruptions that could hurt shareholders and investors personal wealth. Good corporate governance will support the mechanism to control corruptions on the firm level. Indonesia will be prospective and valuable as an investment destination (investment in capital market and foreign direct investment).

Good corporate governance mechanism is essential to help ensure transparency in the conduct of private business. By instigating effective controls and greater transparency in their actions, companies can help address the supply side of corruption, in which money, gifts or other forms of inducement are provided or promised to achieve certain advantages. The results of this research will contribute to improve the understanding about corporate

governance practices on debt policy, the behavior of debt on constraint or facilitate of expropriation and the effect of affiliated ownership issues on debt policy. The empirical results would also provide general indicators of corporate governance, which are useful for both regulator and business people in making debt policy decision as well as in providing certain role of debt on group and no group-affiliate.

Investors will find this research very useful to arrange an investment strategy. The result also helps investors to choose between firms with the best good corporate governance practices especially related to debt as constraint of expropriation. Good corporate governance will enhance the quality of investors' investment value; their quality of life and investment activity. Good governance mechanism such as debt-constraint mechanism also refers to better investors' protections, and the effect of better protections will support the mechanism to minimize corruptions in Indonesia.

The rest of this research study is organized as follows. Part 2 outlines literature study of the role of debt on corporate governance mechanism. This section also presents conceptual framework and develops hypotheses. Part 3 describes research method that consists of sample classification and data requirement, measurement variables and analysis technique. Part 4 contains result and discussion.

2. Literature Review and Hypotheses Development

In this section, the research lays out the theoretical arguments motivating the empirical analysis on the effect of debt on financial performance. The argument will be followed by conceptual framework and hypotheses to be tested.

2.1. The Role of Debt in the Governance Mechanism

Debt policy became a substantial issue on corporate finance since Modigliani and Miller (1958) argued on debt irrelevance to firm value. Their rigid assumption brought many research after them that lessen those assumption. Several theory on corporate finance (Agency Theory, Pecking Order Theory, Signaling Theory, etc.) embrace their argument when lessen several Modigliani and Miller assumption. Modigliani and Miller (1963) complete their argument that tax saving mechanism will increase firm value as debt increase. This research based its argument on Modigliani and Miller (1963) and combined with Agency Theory and recent phenomena on corporate governance practices.

Agency Theory argued that debt would bond expropriation on firm value, and lessen agency conflict between managers and shareholders. As Jensen and Meckling (1976) suggest that agency cost is a trade off model, meaning that if certain agency cost is lower (i.e. agency cost of equity), then other agency cost will rise (i.e. agency cost of debt). As firms more depended on debt as sources of funds, they become more constraint by debt agreement. The agreement was made to constraint managers and shareholders action to

expropriate firm wealth for their own interest. Bondholders or debtholders more highly concern on firm ability to repay their obligation. This research calls the situation as debt-constraint expropriation (DCE).

Other contradicting situations also emerge from debt policy. Debt policy brought debtholders to concern on their investment. On the contrary, managers and shareholders also concern on how to shift their business risk to debtholders. As the result of such thought, managers and shareholders could expropriate cash from debt for their own interest and left debtholders bear all the cost. Firm with enough cash flow as internal sources of fund will use debt instead to support their investment opportunity. Debtholders who are willing to support such a behavior argue that they support a prospective firm with reliable investment opportunity, and internal sources. Those debtholders bear the cost if managers and shareholders exploit debtholders spirit, and use their internal cash flow for their own interest. This research suggests that the condition calls debt-facilitate expropriation (DFE).

2.2. Group-affiliate and No Group-Affiliate Phenomena

Ownership structure of firm also will be divided as group and no group-affiliate firm. Group-affiliate firm is a firm with internal institutional ownership that belongs to the same holding firm (group). No group-affiliate is a stand alone firm with no relation to other firm or holding company. Mahadwartha (2004) introduced the term "internal institutional ownership" to differentiate ownership of institution such as insurance company, mutual fund managers, and other financial services firms, with business institution in non-financial sectors. Indonesian listed firm is known as family firm, because majority of firm belongs to founder's shareholders who have more than 50% ownership. Their ownership is usually on behalf of business institution instead of personal. The facts support the argument that Indonesian firms (and other developing countries) consist of pyramid structure ownership (La Porta, Lopez-de-Silanes, and Shleifer, 1999).

Pyramid structure is usually consisting of several web-connecting firms that end up on behalf of personal ownership calls "ultimate shareholders". This research is not focusing on ultimate shareholders phenomena but on web-connecting firm or group and no group-affiliate.

2.3. Debt-Constraint Expropriation and Debt-Facilitate Expropriation

This research argues that the effect of debt on financial performance moderated by debt characteristic on the expropriation of free cash flow. Firm with Debt-Constraint Expropriation (DCE) will have positive magnitude of debt to financial performance, meanwhile firm with Debt-Facilitates Expropriation (DFE) has a negative magnitude. This research based the argument on the assumption that debt-constraint policy has better expropriation control mechanism than debt-facilitate expropriation. This research also argues that corporate governance embrace debt as value relevance for shareholders and debtholders as well. The hypotheses for DCE (HC) and DFE (HF) are:

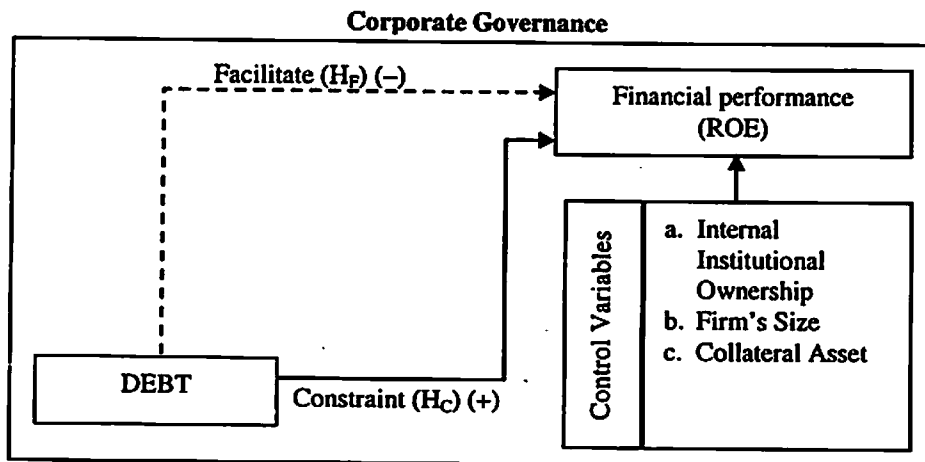
H_C : The effect of debt on financial performance in case of debt-constraint expropriation is positive.

H_F : The effect of debt on financial performance in case of debt-facilitate expropriation is negative.

This research only uses sample with high free cash flow (FCF) to ensure that the sample can be compared between high FCF with high and low debt level. Categorization of DCE and DFE is based on FCF and debt level. Details of measurement are described on methods and analysis section.

The research framework for DCE and DFE conditions is as follows:

FIGURE 1.
Research Framework for DCE and DFE Conditions



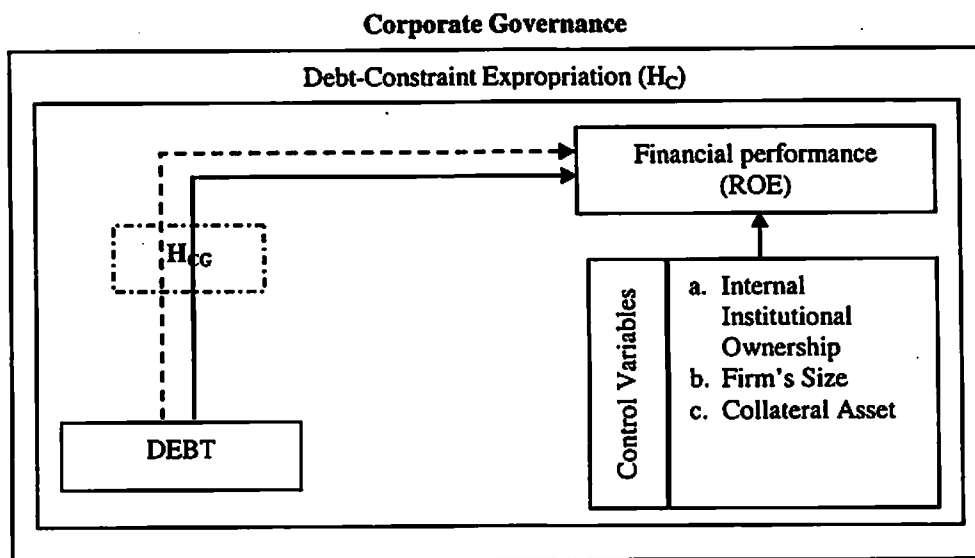
2.4. Group-affiliate and No group-affiliate Hypotheses

As mentioned above, HC hypothesis will test on two different ownership conditions, which are group-affiliate and no group-affiliate. This research argues that DCE's firm with group-affiliate will have less positive effect of debts on financial performance than no group-affiliate firm. The argument is based on assumption that group-affiliate firm will have higher chance to be expropriated by other firm in the same group, although they have debt to constraint such an expropriation. Meanwhile, no group-affiliate firms are relatively free from expropriation and have debt to constraint such an expropriation. The hypothesis for DCE (HCG) on group and no group-affiliate is:

H_{CG} : On DCE condition, the effect of debt on financial performance of group-affiliate firm is positive and lower than no group-affiliate firm.

The research framework for DCE on Group and No group-affiliate is:

FIGURE 2.
Research Framework for DCE on Group and No group-affiliate



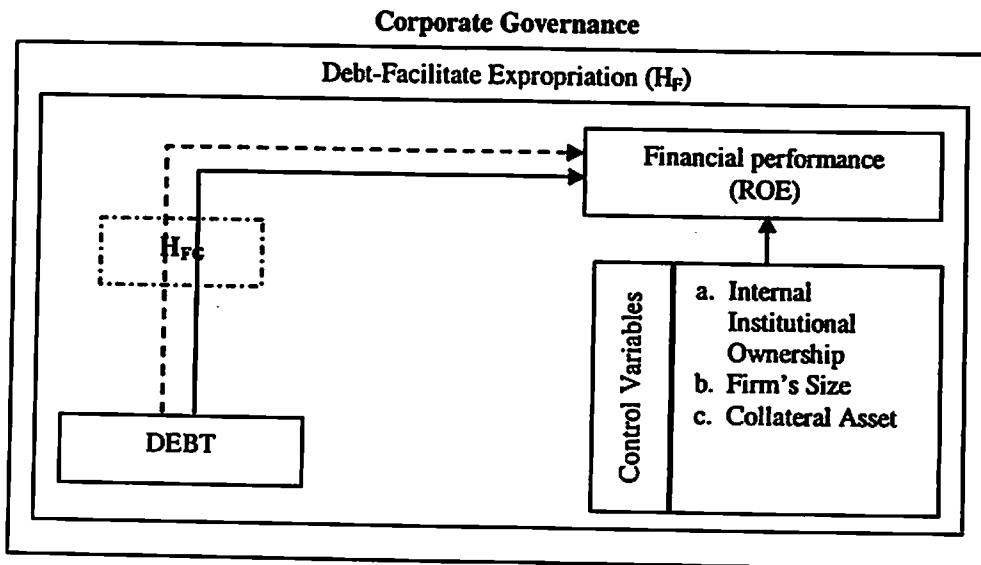
This research argues that DFE will have negative sign on the effect of debt on financial performance. The magnitude of negative effect is higher for group-affiliate than no group-affiliate. The worst condition on DFE becomes severe if the firm is in group-affiliate category, because more chance their resources will expropriate by other parties such as shareholders and managers. Corporate governance mechanism fails to control such an expropriation because the conditions created to support expropriation on firm resources. The hypothesis of DFE (H_{FG}) on group and no group-affiliate is:

H_{FG} : On DFE condition, the effect of debt on financial performance of group-affiliate firm is negative and higher than no group-affiliate firm⁴.

⁴ The word "higher" means the negative effect of debt to financial performance. i.e. the effect of -5 is higher than -1.

The research framework for DFE on Group and No group-affiliate is:

FIGURE 3.
Research Framework for DFE on Group and No group-affiliate



3. Research Method

3.1. Data and Sample

Samples are non-financial Indonesian listed firms with period of analysis from 1995 until 2004. This research will explore several statistical test such as linear regression and Wald test. All statistical tests are based on classical statistic assumptions pre-requirement.

This research eliminates corporations reporting data that are not credible (i.e., negative debt or negative sales) and corporations with missing data on short term debt, long term debt, book or market value of equity, total sales, sales, earning, or income taxes. The ownership structure data on these corporations are taken from Indonesian Capital Market Directory and the network of indirect ownership via other corporations is traced back in order to identify group and no group-affiliate of each firm.

Consolidation forces the assets and liabilities of each subsidiary to be recognized in the accounts of the parent corporation. This can significantly affect the measurement. Rajan and Zingales (1995) noted that, in the year a corporation consolidates its accounts, its debt-to-capital ratio increases, on average, by 5% over the previous year. This suggests that if the sample included a parent corporation with unconsolidated accounts, then this research would typically be under-recording its leverage compared to a similar corpo-

ration with consolidated accounts.

This could bias our results, but not in a direction that is easy to predict. To ensure consistency in the reporting of debt, this research eliminates all corporations reporting unconsolidated accounts, as well as corporations that provided no information about whether or not their accounts are consolidated. This elimination biases our empirical results against the conclusion on debt-facilitate expropriation. This is because some eliminated corporations could have been using debt booked to subsidiaries to expropriate, while avoiding account consolidation legitimately or illegitimately.

This research does not take into account debt between listed corporations and unlisted subsidiaries that it controls in the accounting sense, which is eliminated by consolidation; such a debt is not relevant to agency issues since it is hardly likely to constraint the management of the parent corporation, or to facilitate expropriation in view of its transparency in the consolidated accounts. This research also excludes the unlisted subsidiaries of corporations reporting consolidated accounts, these subsidiaries usually have a few block shareholders and thus are not exposed to the agency problems that are our focus. Non-financial companies do not consolidate account with financial firms, so our debt measures include loans from group bank and financial companies.

3.2. Variables Description

3.2.1. DCE and DFE Criteria for Sub-Sample

This research uses sample with high FCF only. This research divides between high FCF and low FCF using median value of FCF. Then, sample of high FCF will divide between Debt-Constraint Expropriation (DCE), and Debt-Facilitates Expropriation (DFE). This research also uses median value to divide between high and low debt level. Following Table shows categorization for DCE and DCE.

TABLE 1.
DCE and DFE Criteria

Samples are divided into two categories based on DCE and DFE criteria. DCE = Debt-Constraint Expropriation, and DFE = Debt-Facilitates Expropriation. The category is mutually exclusive. The criteria align with 1995 to 2004 period of research analysis. Free Cash Flow (FCF) proxies from Hackel, Livnat, and Rai (1996). Debt is adjusted with Total Assets (TA).

FCF	Debt/TA	Category
High FCF	High Debt	DFE
High FCF	Low Debt	DCE

3.2.2. Group-Affiliate and No Group-Affiliate

A corporation is a “group-affiliate” if it meets one of the four criteria described below. The criteria are:

- a. It is controlled by shareholder(s) via pyramiding, i.e., indirectly through another corporation in the sample;
- b. It is controlling another corporation in the sample;
- c. It has the same controlling shareholder as at least one other corporation in the sample;
- d. It has controlling shareholder, which is corporation or financial institution that is “widely-held” or no shareholder holds 10% or more of the control rights.⁵

Group affiliate variable uses dummy variable of $G = 1$ for the corporation in group-affiliate; and $G = 0$ for no-group affiliate firm. Dummy variable (G) will use to establish interaction variable of debt policy. Interaction variable debt and dummy group (DG) is used to test H_{CG} and H_{FG} .

3.2.3. Free Cash Flow

This study used Hackel, Livnat, and Rai (1996) measurement of FCF with discretionary methods divided by total assets.

$$FCF = \frac{TFCF + DOCO + DCEX}{\text{Total Assets}}$$

$$TFCF = (OCR - OCO) - CEX$$

OCR = *operating cash inflows*

OCO = *operating cash outflows*

CEX = *capital expenditures*

$$DOCO = (OCO \text{ growth} - \text{sales growth}) * (0,2 * OCO)$$

$$DCEX = (CEX \text{ growth} - \text{cost of goods sold growth}) * CEX$$

$$OCO \text{ growth} = (OCOt - OCOt-1) / OCOt-1$$

$$\text{Sales growth} = (\text{Salest} - \text{Salest-1}) / \text{Salest-1}$$

$$CEX \text{ growth} = (CEXt - CEXt-1) / CEXt-1$$

$$\text{Cost of goods sold growth (COGS)} = (COGS t - COGS t-1) / COGS t-1$$

3.2.4. Debt

This research defines debt as the sum of long-term and short-term financial debt divided by total asset. This excludes non-financial liabilities, such as accounts payable,

⁵Such corporations have the same incentive and opportunity to manipulate the corporations that they control as the controlling shareholder of a corporate pyramid. The same definition was used in Claessens et al. (1999b). Khanna and Palepu (2000) use a different definition.

provisions for pensions, deferred taxes, and other provisions for future liabilities.

$$Debt = \frac{Shortterm\ Debt + Longterm\ Debt}{Total\ Assets}$$

This research adjusts each debt ratios for industry and country effects by subtracting the median of the ratio for sample firm in the same industry. This leads to the corporation's industry-adjusted ratios. This adjustment eliminates biases from the industry-specificity of accounting ratios, and inter-firm differences in the way in which accounting items are treated⁶ (La Porta et al., 1997, 1998, 1999, 2000) the effectiveness of the bankruptcy system (Harris and Raviv, 1992; Franks and Torous, 1993); and the tax system (Miller, 1977; King and Fullerton, 1984; Graham, 1996). Thus, this research controls for factors affecting the debt of a specific industry to test whether debt is generally affected by a corporation's vulnerability to expropriation.

3.2.5. Financial Performance

This research uses return on equity as financial performance proxy. Return on equity is performance indicator that is more on the shareholders side. Shareholders concern on their investment on the firm, which is represented by the return on equity. The equation for return on equity is:

$$ROE = \frac{EAT}{Equity}$$

Where; EAT = earnings after tax; Equity = book value of equity

3.3. Control Variables

This research uses three control variables (Internal Institutional Ownership, Firm's Size, and Collateral Asset). The variables are as follows:

- a. **Internal institutional ownership:** Firm with high internal institutional ownership has higher performance than low internal institutional ownership (Mahadwartha, 2004).
- b. **Firm Size:** This is measured by the logarithm of the corporation's total assets, Ln(TA). Rajan and Zingales (1995) argue that size could proxy for the probability of default, which is higher for smaller firms. On the other hand, larger, more visible firms suffer less from informational asymmetry, have easier access to equity markets and, therefore, should be less levered, and higher financial performance. Mixed evidence is provided by Hoshi, Scharfstein and Kashyap (1990), Kester (1986),

⁶See Rajan and Zingales (1995) for a discussion of these practices, and an analysis of differences in leverage across the G-7 countries.

- Kim and Sorensen (1986), and Rajan and Zingales (1995).
- c. **Collateral Asset:** Asset tangibility is measured by the ratio of fixed to total assets. Rajan and Zingales (1995) argue that fixed assets are easier to collateralize, and so reduce the agency costs of debt. The reduction of agency cost of debt will increase firm financial performance. However, Berger and Udell (1994) argue that this relationship would be weaker in relationship-oriented economies.

3.4. Empirical Models

This research uses one independence variable (Debt; D), one dependence variable (financial performance; FP), three control variables (Internal Institutional Ownership – IIO; Firm’s Size – FS; and Collateral Asset – CA), and categorization between DCE and DFE; and group and no group-affiliate (G). The main equation for DCE and DFE sub-samples are as follows:

$$FP_{iDCE} = \alpha + \beta_{11}D_{iDCE} + \beta_{12}IIO_{iDCE} + \beta_{13}FS_{iDCE} + \beta_{14}CA_{iDCE} + \epsilon_{iDCE} \tag{1}$$

$$FP_{iDFE} = \alpha + \beta_{21}D_{iDFE} + \beta_{22}IIO_{iDFE} + \beta_{23}FS_{iDFE} + \beta_{24}CA_{iDFE} + \epsilon_{iDFE} \tag{2}$$

The equation for test DCE and DFE for group and no group-affiliate is:

$$FP_{iDCE} = \alpha + \beta_{31}D_{iDCE} + \beta_{32}IIO_{iDCE} + \beta_{33}FS_{iDCE} + \beta_{34}CA_{iDCE} + \beta_{35}G_{iDCE} + \beta_{36}D_iG_{iDCE} + \epsilon_{iDCE} \tag{3}$$

$$FP_{iDFE} = \alpha + \beta_{41}D_{iDFE} + \beta_{42}IIO_{iDFE} + \beta_{43}FS_{iDFE} + \beta_{44}CA_{iDFE} + \beta_{45}G_{iDFE} + \beta_{46}D_iG_{iDFE} + \epsilon_{iDFE} \tag{4}$$

The research uses ordinary least square regression (OLS) with preliminary testing on classic regression assumption. Wald test will uses as coefficient test between group and no group-affiliate on DCE and DFE sub-sample. The hypotheses tests are shows in Table 2.

TABLE 2.
Hypotheses Testing

H _C :	The effect of debt to financial performance when debt-constraint expropriation is positive.	0 < β ₁₁
H _F :	The effect of debt to financial performance when debt-facilitate expropriation is negative.	β ₂₁ < 0
H _{CG} :	On DCE condition, the effect of debt to financial performance on group-affiliate firm is positive and lower than no group-affiliate firm.	0 < β ₃₁ 0 < β ₃₁ + β ₃₆ β ₃₁ + β ₃₆ < β ₃₁
H _{FG} :	On DFE condition, the effect of debt to financial performance on group-affiliate firm is negative and higher than no group-affiliate firm.	β ₄₁ < 0 β ₄₁ + β ₄₆ < 0 β ₄₁ + β ₄₆ < β ₄₁

4. Result and Discussion

The results are organised as follows. First, the results show descriptive statistics for independent variable (Debt; D), dependent variable (financial performance; FP), control variables (Internal Institutional Ownership – IIO; Firm's Size – FS; and Collateral Asset – CA), and categorization between DCE and DFE; and group and no group-affiliate (G). Second, this research shows regression results for each of the category. Third section is discussion and suggestion.

4.1. Descriptive Statistic

This research uses pooling data with 1,559 firm-year observations and 158 firms from 1995 until 2002, 148 firms for 2003, and 147 firms for 2004. The period of analysis is 1994 to 2004; however, this research uses growth model of free cash flows, and year 1994 is use to calculate the growth of 1995⁷. Table 3 shows sample between high and low free cash flow, then split of high free cash flow sample into high and low debt to determine two categories of Debt-Constrain Expropriation (DCE) and Debt-Facilitate Expropriation (DFE). Table 3 also showed group and non-group affiliated firms among high free cash flow firms. The result suggest that majority of listed firms are group affiliated, therefore vulnerable to expropriation from affiliate firms or owners.

TABLE 3.
High Free Cash Flow, DCE and DFE, Group and Non-group

Sample divided into Low free cash flow, and high free cash flow. High free cash flow also divided into DCE and DFE, and group affiliated and non-group affiliated firms.

Variable	Firm Year	%
Low Free Cash Flow	779	49.97%
High Free Cash Flow:	780	50.03%
Debt-Constrain Expropriation (DCE)	390	50%
Debt-Facilitate Expropriation (DFE)	390	50%
Group and Non-group affiliated:		
Group affiliated (G=1)	735	94.23%
Non-group affiliated (G=0)	45	5.77%

Table 4 shows descriptive statistics of Debt-Constraint Expropriation (DCE) and Debt-Facilitate Expropriation (DFE). The table shows that each category has 390 observations. Financial performance variable (ROE) shows the highest negative minimum value

⁷This method subtracts firm-year observations from 1.717 to 1.559.

for DCE category. Collateral assets for DFE also show the highest value of standard deviation.

TABLE 4.
Descriptive Statistic

Descriptive statistic divides into two categories that are Debt-Constraint Expropriation (DCE) and Debt-Facilitate Expropriation (DFE). Debt (D), Firm performance (FP), Internal Institutional Ownership (IIO), Firm's Size (FS), and Collateral Asset (CA).

Debt Constrain Expropriation (DCE)	FP	D	IIO	FS	CA
Mean	0.040	0.041	0.525	26.298	1.950
Median	0.085	0.046	0.592	26.496	0.724
Maximum	2.971	0.075	0.592	28.076	9.445
Minimum	-3.166	0.003	0.000	24.060	0.001
Standard Deviation	0.596	0.020	0.143	0.855	2.300
Observations	390	390	390	390	390
Debt-Facilitate Expropriation (DFE)	FP	D	IIO	FS	CA
Mean	0.142	0.839	0.638	27.565	3.105
Median	0.186	0.403	0.673	27.598	0.263
Maximum	0.187	28.472	0.973	31.444	218.199
Minimum	0.001	0.185	0.000	24.232	0.000
Standard Deviation	0.061	2.084	0.204	1.481	14.781
Observations	390	390	390	390	390

4.2. Regression Result and Wald Test

Table 5 shows regression result for first equation of Debt Constrain Expropriation (DCE). The result shows that only IIO insignificant and other variables significant ranging from alpha 1% to 10%. Coefficient of debt is positive 4.035, which indicates that Hypothesis H_c hold. Higher debt will increase firm performance.

TABLE 5.-
Regression Result for H_c

Equation 1 contains of one main independent variable which is Debt and three control variables. The dependent variable is financial performance (FP).

Variable	Coefficient	t-Statistic	
Constant	-2.639	-2.780	***
β_{11} DEBT	4.035	2.191	**
β_{12} IIO	0.016	0.098	
β_{13} FS	0.094	2.645	***
β_{14} CA	0.022	1.931	*
	R-squared	0.037	

Table 6 shows regression result for second equation of Debt-Facilitate Expropriation (DFE). The result shows that FS and CA insignificant and other variables significant ranging from alpha 1% to 10%. Coefficient of debt is positive 0.002, and significant 1%, which indicates that Hypothesis H_F rejected. Higher debt will increase firm performance.

TABLE 6.
Regression Result for H_F
Equation 2 contains of one main independent variable which is Debt and three control variables. The dependent variable is financial performance (FP).

Variable	Coefficient	t-Statistic
Constant	0.171	2.881 ***
β_{21} DEBT	0.002	1.856 *
β_{22} IIO	-0.022	-1.679 *
β_{23} FS	-0.001	-0.272
β_{24} CA	0.000	0.687
	R-squared	0.012

The research argument of debt-facilitate expropriation when debt level high is not hold. However, the magnitude of debt coefficient of DCE is higher than DFE category. This result suggests that DCE have more positive effect to constraint expropriation rather than DFE category.

Table 7 shows the regression for equation 3, the group and no-group related and the interaction with debt. The result shows that H_{CG} significantly holds that partially confirm debt have positive effect on performance when debt-constraint expropriation happened. Two more test conducted to test the robustness of the hypothesis. Wald test chooses as coefficient test for H_{CG} .

TABLE 7.
Regression Result for H_{CG}
Equation 3 contains of three main independents variable, which are Debt, dummy group and no- group, and the interaction. The dependent variable is financial performance (ROE).

Variable	Coefficient	t-Statistic
Constant	-2.630	-2.777 ***
β_{31} DEBT	4.935	2.384 **
β_{32} IIO	0.222	0.456
β_{33} FS	0.093	2.612 ***
β_{34} CA	0.022	1.820 *
β_{35} G	-0.098	-0.387
β_{36} DG	-0.651	-0.894
	R-squared	0.040

Table 8 shows Wald test on H_{CG} when there is group and no-group condition amongst DCE firms. The effect of debt to performance is positive as predicted. However, the magnitude is lower on group-affiliate firm rather than no group-affiliate. The result also shows that constraint to expropriation more effective on no group-affiliate firm than group-affiliate firms.

This research argues that firm with no group-affiliate will have independency to manage and control their firms. As independency increase, firm with DCE will be able to use efficient financial resources, especially from debt policy. Group-affiliate firms will have higher chance to expropriate by other firm in the same group, although they have debt to constraint such expropriation.

TABLE 8.
Wald test of H_{CG}

Wald is a test for coefficient of regression based on several constraints.

Test Statistic	Value
$0 < \beta_{31}$	4.935
t-statistic	2.384 **
$0 < \beta_{31} + \beta_{36}$	4.284
F-statistic	5.343 **
$\beta_{31} + \beta_{36} < \beta_{31}$	-0.651
F-statistic	0.799

Table 9 and Table 10 show regression result and Wald test of H_{FG} . The regression result shows that debt policy on facilitated expropriation firms will have negative effect on firm performance. This preliminary result diverges with OLS regression result on Table 6. However, this result concord with the hypothesis H_F and the first step of Wald test on hypothesis H_{FG} . The Wald test on hypothesis H_{FG} comes with three steps (the same as H_{CG}).

TABLE 9.
Regression Result for H_{FG}

Equation 4 contains of three main independents variable, which are Debt, dummy group and no-group, and the interaction. The dependent variable is financial performance (ROE).

Variable	Coefficient	t-Statistic
Constant	0.1861	3.1081 ***
β_{41} DEBT	-0.0186	-6.4003 ***
β_{42} IIO	-0.0188	-1.0190
β_{43} FS	-0.0004	-0.1856
β_{44} CA	0.0002	2.4309 **
β_{45} G	-0.0234	-1.6328
β_{46} DG	0.0205	7.1809 ***
R-squared		0.0217

Table 10 shows three steps of Wald test on H_{FG} . The result shows that all three steps confirms with Wald, ranging from 5% to 10% significant level. Debt of firms that facilitated expropriation and group-affiliate will have negative effect on performance. Higher debt to expropriate will lower firm financial performance.

The result also shows that the effect (magnitude of coefficient) of debt to performance is higher on no group-affiliate firms than group-affiliate firms are. The result diverges from H_{FG} , which argues that the negative magnitude of debt to performance is higher for group-affiliate than no group-affiliate. This research argues suggest that deviation from hypothesis H_{FG} result from risk reduction mechanism of diversification.

TABLE 10.
Wald test of H_{FG}

Wald is a test for coefficient of regression based on several constraints.

Test Statistic	Value
$\beta_{41} < 0$	-0.0186
t-statistic	-6.4003 ***
$\beta_{41} + \beta_{46} < 0$	0.0019
F-statistic	4.665 **
$\beta_{41} + \beta_{46} < \beta_{41}$	0.0205
F-statistic	51.565 ***

Risk reduction mechanism of diversification resulted from firm with group-affiliate that can reduce their overall risk with diversify business risk amongst within groups. However, the suggestion needs further examination trough in-depth future research.

4.3. Discussion and Suggestion

Research on debt-constraint or facilitated expropriation is the first in-depth research for Indonesian firms, especially firms that listed on Jakarta Stock Exchange. This research proposes the term of debt-constraint expropriation (DCE) and debt-facilitated expropriation (DFE); and verifies and tests issue on expropriation of debt policy. The result shows sufficient evident that constraint and facilitated expropriation on debt is meaningful with regard to financial performance. Firms on debt-constraint expropriation condition, then debt policy will have positive effect on financial performance. On the contrary, debt-facilitated expropriation condition, then debt policy will have negative effect on financial performance. Expropriation on debt is damaging overall firm value, however will increase personal wealth of agent and principal of the firm.

Further analysis tested the differences of debt-constraint expropriation and debt-facilitate expropriation on no group-affiliate and group-affiliate firms. Group and no group-affiliate represent the power of principal to elaborate the scheme of expropriation and sufficiently harm debtholders value. On debt-constraint expropriation, no group-affiliate firms will have higher positive effect of debt to performance than group-affiliate firms

are. This research shows that no group-affiliate firms have independency to manage and control their firms. As independency increase, firm with debt-constraint expropriation will be able to use efficient financial resources, especially from debt policy. Group-affiliate firms will have higher chance to expropriate by other firm in the same group, although they have debt to constraint such expropriation.

On debt-facilitate expropriation, this research shows contradict result. Firms with group-affiliate will have more chance to engage in risk reducing mechanism trough diversification than firm with no group-affiliate. Risk reduction mechanism of diversification resulted from firm with group-affiliate that can reduce their overall risk with diversify business risk amongst within groups.

Debt as bonding and monitoring on corporate governance practices, shows reliable system to reduce expropriation on minority shareholders and even debtholders value. Ownership affiliation also plays a major rule on expropriation of minority shareholders and debtholders. However, group-affiliate ownership has an advantage to diversify their risk of expropriation. This research suggests that no group-affiliate could engage in strategic partner or trade organization to cover their risk of expropriation.

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DEBT POLICY, FREE CASH FLOW HYPOTHESIS, AND BALANCING OF AGENCY THEORY THROUGH OWNERSHIP: EVIDENCE FROM INDONESIA

Putu Anom Mahadwartha*, Fitri Ismiyanti**

Abstract

This research argues that there is conflict of interest between managers and shareholders. The conflict also varies based on growth opportunities. This research argues that disciplinary role exist in debt policy with the use of free cash flow hypothesis. This research explores the implications of free cash flow hypothesis concerning the disciplinary role of ownership structure in corporate debt policy. Managerial ownership and internal institutional are other mechanism to reduce agency conflict also has a significant impact on debt policy (control coalition cohesiveness). The relationship between managerial ownership and debt policy is interdependence, as known as balancing of agency theory. This study uses 1264 observation of 154 listed Indonesian firms between the years 1995 until 2003. Three state least square (3SLS) model will be use for statistical and analytical purposes. This study developed several arguments. The relation between debt and free cash flow are positive, but the relation differs between low-growth firms and high-growth firms. Internal institutional shareholders discourage managerial perquisites using debt. The result of this research support the free cash flow hypothesis and balancing of agency theory through ownership and there is disciplinary role of ownership structure in debt policy.

Keywords: Balancing of Agency Theory, Ownership Structure, Leverage, Free Cash Flow, Agency Conflict

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1. Introduction

The agency costs of free cash flow arise from a conflict between manager and shareholders. When managers insulate themselves from internal and external governance mechanism, they have incentives to pursue their own interests at the expenses of shareholders, e.g. higher than market salaries, excessive perquisites⁷, job security. Managers also tend to value investment even if the investments can not maximize shareholders value since managers gain prestige being the managers of a big firm (this behavior is known as overinvestment problem). Jensen (1986) discussed the agency cost of free cash flow as cash flow in excess that required funding all projects that have positive net present value (NPV).

According to Jensen (1986), manager may use free cash flow to invest in negative NPV projects rather than return the free cash flow to the shareholders, for example as dividends. This problem especially worsens in firms with maturity life cycle and has few growth opportunities, as they have few profitable investments. However, using required interest payments, manager is bonding their promise to pay out future cash flows. Jensen (1986) indicates that firms with excess cash flows and low growth opportunities will use more debt financing for monitoring and bonding purposes.

Indonesian evidence regarding the issue of bonding and monitoring from debt are also tested by Mahadwartha (2002a, 2002b, 2003, and 2004), Ismiyanti and Hanafi (2004), and Mahadwartha and Hartono (2003). Majority of findings support Jensen's argument that debt is bonding and monitoring mechanism in agency conflict. Conflict of interest between managers and shareholders will bond by

⁷ Perquisites are luxury office building, luxury transportation and accommodation beyond their jobs standard, etc.

fixed interest payment, and monitor by debt covenant that attach to debt agreement.

Shleifer and Vishny (1986) argue that shareholders have an incentive to monitor managers as their investment at stake. Pound (1988) suggests that institutional investors serve as an alternative mechanism to control the overinvestment problem. Agrawal and Mandelker (1990) indicate that institutional investors provide valuable monitoring services and act as a restraint to opportunistic behavior by managers. Thus, institutional investor may help in reducing the firm's agency cost and become a substitute for debt if institutions can monitor managerial activities at a low cost. This research tries to investigate the implications of free cash flow hypothesis on capital structure policy especially debt policy of listed Indonesian firms.

Mahadwartha (2004) introduces the term "internal institutional" as major investors in Indonesia. Indonesia have different investors' demography especially for institutional investor. As Pound (1988), and Agrawal and Mandelker (1990) define institutional investor as investment company, insurance company, and other institutional investors with line of business on investment or managing investment fund from clients. There is no recorded and published data regarding ownership of institutional investors such as insurance companies, mutual funds, etc in Indonesian public firms. Mahadwartha (2004) then define institutional investors in Indonesia as business firm that have portions of ownership in listed firms. Business firms include not only as Pound (1988), and Agrawal and Mandelker (1990) defined, but also usual business firms.

Mahadwartha (2004) argues that internal institutional investors serve as a mechanism to bonding and monitoring managers' perquisites behavior. The findings support the argument that firms with large portions of internal institutional ownerships have better financial performance than firms with small portions of internal institutional ownerships have. Balancing of agency theory argues that ownership structure as bonding will have substitution effect with other bonding mechanism such as debt and dividend. This research argues that managerial ownership will have a substitution on debt but internal institutional will have positive effect. Managers as their ownership increase will consider reducing firms' liabilities in order to decrease firm financial risk. Furthermore, when debt is increasing, then managers will decrease their ownership portions to decrease their personal investment risk.

Internal institutional ownership in Indonesia usually business firm that affiliated closely to founders of the firms. As internal institutional increase, founders have a better chance to control firms' managers regarding cash flow. In Indonesian cases, balancing of agency theory will hold on the relationship between internal institutional ownership and debt policy. Ownership structure such as

managerial ownership and internal institutional ownership will have substitution affect, as a mechanism to reduce agency conflict. Balancing of agency theory will also hold on the mechanism through ownership structure. On the contrary, control coalition cohesiveness as oppose to balancing of agency theory will not hold. Regardless, the differences of level of cohesiveness between types of ownership structure, managerial ownership and internal institutional ownership will have partially coherent interest. Other argument is internal institutional ownership as majority parties have superior power to control managers and their perquisites actions.

Free cash flow as sources of manager's perquisites will have a positive effect on debt, because shareholders will bond manager's perquisites to the use of debt. High growth and low growth firm will have different effect on the relationship of free cash flow to debt policy. This research argues that the relationship of free cash flow to debt will have positive effect when firm in low growth conditions and negative effect when firms in high growth conditions. Firms with lower level of growth will have redundant cash flow that could be use by managers for perquisites. Then, shareholders will bind manager's perquisites using debt policy. On the contrary, high growth firms if they have lower level of cash flow, shareholders will use debt to finance their investment opportunity.

This research focuses on relations between debt, free cash flow, managerial ownership, institutional internal ownership, and growth. This research also examines the relationship between different types of ownership to debt policy; both are serving as monitoring mechanism for agency conflict. The interest in studying Indonesian firms stems from some factor. The ownership structure of Indonesian firms is quite different from other countries. Indonesian firms dominated with family firms and conglomerate with significant portions of ownership and only small portions of other shareholders.

Two features distinguish this study. First, it provides evidence consistent with free cash flow hypothesis predictions in a legal and regulatory environment that is different from the United States. Second, previous research such as Mahadwartha (2004) is focus only on the degree of institutional ownership. However, the characteristics and intensity of monitoring may vary across institutional investors to affect corporate debt policy. Given the prevalence of internal institutional ownership in Indonesian firms (Mahadwartha, 2004), the research focuses on the bonding and monitoring mechanism of free cash flow to debt on two separable conditions, low growth and high growth firms.

This study also enhances our understanding on the effect internal institutional ownership structures to debt policy, the interdependence of managerial ownership and debt policy, and the relationship of internal institutional ownership to managerial

ownership. Balancing of agency theory argues that ownerships as mechanism for reducing agency conflict have a substitute effect on debt policy, dividend policy, and on different type of ownership (which is also the mechanism of agency conflict). Mahadwartha (2002) confirm the balancing model of agency theory, and support such relationship. Ismiyanti and Hanafi (2004) also find a significant relationship to support the balancing of agency theory between debt policy, dividend policy, and ownership structure.

1.1. Research Problems

Four research problems will describe based on the research argument. The research problems are as follows:

- a. Is balancing of agency theory hold on the relationship between managerial ownership and debt policy?
- b. Is free cash flow affect debt policy?
- c. Is the effect of free cash flow to debt policy differing between high growth firm and low growth firm?
- d. Is balancing of agency theory hold on the relationship of internal institutional ownership to debt policy?
- e. Is balancing of agency theory hold on the relationship of internal institutional ownership to managerial ownership?

1.2. Research Original

The research has two original ideas. Firstly, the originality of the research is on testing the low and high growth condition on the effect of free cash flow to debt policy. This research argues that the relationship of free cash flow to debt policy moderates by growth level. The research also develops new argument regarding this matter based on agency theory perspective. Secondly, the research argues that the balancing of agency theory will hold on the interdependence relationship between managerial ownership to debt policy, on the relationship between institutional ownership to debt policy, and on the relationship between internal institutional ownership to managerial ownership. The argument based on unique agency problems in Indonesia, which this research introduces as control coalition cohesiveness.

1.3. Research Contribution

This research has three major contributions on empirical, methodology, and policy. The research support previous empirical research in Indonesia regarding balancing of agency theory, and enhance the argument to test growth and low growth conditions. The research also tests the effect of ownership structure issues to debt policy in Indonesia

and introduce control coalition cohesiveness hypothesis.

The research findings contribute to investors' decision on their personal investment policy. Investor will have sufficient information regarding firm's agency conflict that can jeopardize their investment decision. Regulators will have better understanding on free cash flow as source of perquisites and will regulate such matters accordingly.

2. Literature Review and Hypotheses

The research tests three main arguments with regard to free cash flow, balancing of agency theory, control coalition cohesiveness, and growth hypothesis. This research will divide the argument into two parts and four hypotheses.

2.1. Free Cash Flow Hypothesis and Growth Hypothesis

Jensen (1986) identified the conflict between the shareholders' interests and the managers' individual agendas and suggested the debt is a remedy against this form of agency cost, as debt forces the company to pay out the excessive cash flow; it decreases the free cash flow, which is at managers' discretion and thus in danger of being sub optimally invested. Stulz (1990) shows that optimal for shareholders to increase leverage when managers have personal objectives.

There are some previous studies investigates the free cash flow issues. One strain of empirical work examines the overinvestment problem by analyzing the relation between growth opportunities and free cash flow on the one hand, and free cash flow with leverage on the other hand. They showed negative relationship between debt and growth opportunities (Smith and Watts, 1992; and Lang, Ofek and Stulz, 1996) and changes in free cash flow lead to positive changes in leverage (Crutchley and Hansen, 1989). Another approach to the implications of the free cash flow hypothesis in corporate capital structure policy is to study specific events regarding capital structure policies. Several researches in general showed that the firms acted according to free cash flow theory (Denis and Denis, 1993; and Blanchard, Silanes, and Shleifer, 1994). Shareholders will bind manager's perquisites action with increase on debt. They will "invite" such parties (debtholders) to monitor and control managers' perquisites using debt covenant. This argument calls free cash flow hypothesis.

H1a: Free cash flow will positively affect debt policy

This research also argues the differences between low growth and high growth firms on the relationship of free cash flow to debt policy. Lang, Ofek and Stulz (1996) showed negative relationship between growths to debt policy. Firms with high growth firms will have lower debt policy because growth firm usually

inherited higher risk than low growth firms did. High-risk levels will reluctant debtholders to finance firms' investment. This research has rather different argument than Lang, Ofek and Stulz (1996).

This research argues that firm with low level of cash flow and on the stage of high growth will have high debt level to finance their growth opportunities. Firms with high growth level will have negative relationship between free cash flow to debt policy. Firms with high growth level will finance their growth using internal cash flow before debt. Firms with low growth level will have positive relationship between free cash flow to debt policy. Shareholders will bind free cash flow with debt policy, explicitly through debtholders using debt covenant. Therefore, shareholders of low growth firms will have higher interest to bind free cash flow from manager's perquisites using debt policy. The argument also holds for debt policy as monitoring mechanism for manager's actions. This argument calls growth hypothesis.

H1b: High growth firms will have negative relationship between free cash flow to debt policy, on the contrary to low growth firms.

2.2. Balancing of Agency Theory and Control Coalition Cohesiveness

Managers hired by the stockholders through the Board of Directors to run the firm in the shareholders' best interests. Thus, owners (shareholders) differ from the agent (management) engaged in the day-to-day decision-making regarding the allocation of firm's resources. The advantages of such separation are that shareholders can specialize in risk bearing while managers specialize in managing the corporation. Owners unnecessarily have to know regarding how to manage a firm thus resulting in a wider spreading of ownership since the option to buy shares is available to everybody. Major disadvantages are that managers tend to strive for goals that are sometimes inconsistent with the shareholder goals. This results in the arousal of agency problems where agents do not maximize their effort or do not use all of their skills and resources⁸. Furthermore, adverse selection is taking place, meaning that agents misrepresent their abilities to their principals.

Jensen and Meckling (1976) argue that managerial ownership reduces managerial incentives to engage in such no optimal behavior describe above. As managerial ownership increases, managers bear more of the wealth effects on their divergent behaviors. As agency theory argued that ownership structure (managerial ownerships, institutional ownership, etc), debt policy, and dividend policy are main mechanism in controlling managers' action (Mahadwartha, 2004). Such mechanism will have

substitution effect as each mechanism has substantial cost.

Balancing of agency theory predict that shareholders concerns about the cost occur from conducting such mechanism to control agency conflict. Thus, the disciplinary pressures of debt and managerial ownership are substitutes. Some previous studies found significant negative relation between debt and managerial ownership (Friend and Lang, 1988; Jensen, Solberg, and Zorn, 1992; Chen and Steiner, 1999; Mahadwartha, 2004; and Ismiyanti and Hanafi, 2004). Tandelilin (2003) showed significant interdependence relationship between managerial ownership and debt policy, which is conclude that balancing of agency theory hold.

H2: There is an interdependence negative relationship between managerial ownership and debt policy

Shleifer and Vishny (1986), and Pound (1988) suggest that institutional investors serve as an alternative mechanism to control the overinvestment problem. Institutional investors have greater expertise mechanism to control the overinvestment problem. Institutional investors have greater expertise in gathering and interpreting information on firms, and have more incentives closely oversee managerial activities with an increase in their equity ownership. This implies that institutional investors impose their managerial preferences through the governance process. Some evidence suggests that there is a negative relationship between institutional ownership and debt policy (Crutchley and Hansen, 1989; Bathala, Moon and Rao, 1994).

However, Mahadwartha (2004) argues that Indonesia have a unique agency problems especially regarding institutional ownership. In Indonesia, institutional ownership usually own by founding family ownership through business firm (PT-Ltd; *perseroan terbatas*-limited) and they dominate the ownership structure with average of 48% from 1995 until 2002. Mahadwartha (2004) introduced the term "internal institutional ownership" to comply with the evident of Indonesian firms.

This research argues from coalition control cohesiveness point of view that the level of cohesiveness of ownership will affect the magnitude of influences each ownership structure to other agency conflict mechanism. Indonesian firms as describe by Mahadwartha (2004) shows several differences on ownership issues than developed countries firms. Mahadwartha (2004) to overcome such differences and test it in scientific research introduced the term internal institutional ownership. This research argues that firms with high level of internal institutional ownership will have low debt level. Internal institutional shareholders will have more control on managers' action and will conduct effective control mechanism. Firms will concern on

⁸ Sometime refer as moral hazard

cost of such mechanism therefore balancing of agency theory will holds on such situation.

H3: *Internal institutional ownership will negatively affect debt policy*

This research also tests other balancing of agency theory especially on ownership structure. Ownership structure as control mechanism will also have substitution relationship between other ownership structures. This research tests the relationship between

institutional ownership to managerial ownership. Crutchley, Jensen, Jahera, and Raymond (1999) examine such relationship and found a negative affect or support balancing of agency theory.

H4: *Internal institutional ownership will negatively affect managerial ownership.*

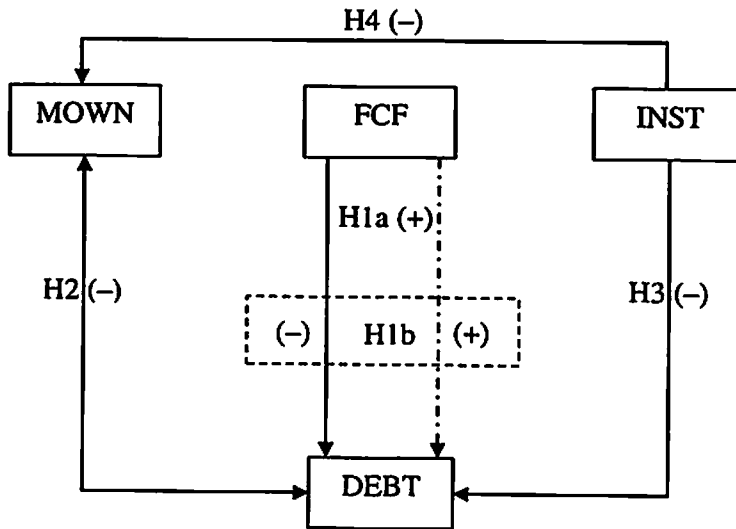


Figure 1. Research Framework

Note:

————> = High growth firm (D=1)

-----> = Low growth firm (D=0)

MWON = managerial ownership

FCF = free cash flow

INST = internal institutional ownership

DEBT = debt policy

3. Research Methods

3.1. Sample and Data

This research uses secondary data. The data collected from financial statements for periods of analysis of 1995 - 2003. Sources of data are Jakarta Stock Exchange library, Indonesian Capital Market Directory (ICMD), and Indonesian Securities Market Database (ISMD) Gadjah Mada University. This research employs 147 listed firms from Jakarta Stock Exchange (JSX) and geographically operates in Indonesia.

3.2. Operational Definition and Variables Measurement

This research employs two endogenous variables, three exogenous variables, and three control variables. Endogenous variables are:

1. Debt policy (DEBT) is proxy from long-term debt to total asset (Mahadwartha, 2004).

$$DEBT_u = \frac{Total.Debt_u}{Total.Assets_u}$$

2. Managerial ownership (MWON) is proxy from proportions of ownership managers' own (in percentage basis).

Three exogenous variables are use for this research based on conceptual arguments of agency theory and support by several empirical researches. Such variables are as follows:

1. Dummy low and high growth (D): this research employ interaction between dummy (D) with free cash flow variables to test growth hypothesis. D=1 for high growth firms and D=0 for low growth firms. Growth proxies from asset growth:

$$Growth.Assets_u = \frac{Asset_u - Asset_{u-1}}{Asset_{u-1}}$$

Asset data for 1994 will need to fulfill the growth level in 1995. Median of growth level will use as divider for low growth (D=0) and high growth firms (D=1).

- Free cash flow (FCF): This study used Hackel, Livnat, and Rai (1996) modified and divided by total assets.

$$MFCF = (OCR - OCO) - CEX$$

MFCF = modified free cash flow

OCR = operating cash inflows

OCO = operating cash outflows

CEX = capital expenditures

$$FCF_u = \frac{MFCF_u}{Total.Assets_u}$$

- Internal institutional ownership (INST): Internal institutional ownership proxies from proportions of ownership internal institution own (in percentage basis).

Four control variables are use for this research based on several previously Indonesian empirical researches. Such variables are as follows:

- Crisis period (DCrisis): Miller (1998), and Hahm and Mishkin (2000) shows that micro variables could predict crisis period in Asia with more accurate level than macro variables. Dummy crisis period proxies from 1995-1997 (D=0) and 1998-2003 (D=1). Several previous empirical researches in Indonesia such as Mahadwartha (2002a), Mahadwartha (2002b), Mahadwartha (2003), Mahadwartha and Hartono (2002), Tandililin (2003), and Mahadwartha (2004) support the use of crisis period as control variable.
- Firm size (SIZE): Gaver and Gaver (1993), Tandililin (2003), and Mahadwartha (2004) show a positive relationship between size and debt policy. Size proxies as follows:

$$SIZE_u = \frac{Fixed.Assets_u}{Total.Asset_u}$$

- Dividend policy (DIV): dividend payout ratio proxies with dummy variable (D=1 for paying dividend; and D=0 for non-paying dividend). Tandililin (2003), and Mahadwartha (2004) showed significant relationship of dividend with debt policy. As one of control mechanism for agency conflict, dividend supposedly has substitutive relationship with debt policy (balancing of agency theory).
- Return on Asset (ROA): Bathala, Moon dan Rao (1994), and Ismiyanti and Hanafi (2004) examine the relationship of return on asset to debt policy and found a significant relationship. This research uses ROA as control variables on managerial ownership. This research argues that managers' will concern on return on asset rather than return on equity (shareholders side) as agency theory assume self interest behavior in managers actions.

$$ROA_u = \frac{Net.Income_u}{Total.Asset_u}$$

3.3. Methods of Analysis

This research uses three stage least squares (3SLS) to test the relationship of endogenous and exogenous variables. Three-stage least squares (3SLS) is the two stage least squares (2SLS) version of the Seemingly Unrelated Regression (SUR) method. It is an appropriate technique when right-hand side variables correlated with the error terms, and there is both heteroskedasticity, and contemporaneous correlation in the residuals. 3SLS require the problems identification for research equation (Gujarati, 2003: 735). Wald test also implement to test the differences between coefficient of free cash flow to debt policy and the interaction coefficient of free cash flow with growth level. Wald test will confirm the hypothesis H1b.

The research equations are:

Equation 1:

$$DEBT_u = \alpha_1 + \beta_{11}FCF_u + \beta_{12}FCF_u * D + \beta_{13}MOWN_u + \beta_{14}INST_u + \beta_{15}SIZE_u + \beta_{16}DCrisis_u + \beta_{17}DIV_u + \epsilon_u$$

Equation 2:

$$MOWN_u = \alpha_2 + \beta_{21}DEBT_u + \beta_{22}DIV_u + \beta_{23}SIZE_u + \beta_{24}DCrisis_u + \beta_{25}ROA_u + \beta_{26}INST_u + \epsilon_u$$

Identification problem conduct as follows:

K = all variables from the equation (endogenous and exogenous) including control variables (total of eight variables).

k = variables on the equation;

Equation 1: k = DEBT, FCF, D, MOWN, INST, SIZE, DCrisis, and DIV;

Equation 2: k = MOWN, DEBT, DIV, SIZE, DCrisis, ROA, and INST.

m = endogenous variable = DEBT, and MOWN.

The rules for identification problems:

K - k ≥ m - 1: over identified

K - k = m - 1: exactly identified

K - k ≤ m - 1: unidentified

Results from identification problems:

Equation 1: 9 - 8 = 2 - 1; exactly identified

Equation 2: 9 - 7 ≥ 2 - 1; over identified

As the two equations are exactly and over identified then 2SLS can be employ on these equations properly.

4. Result and Discussion

Table 1 shows a descriptive of nine endogenous and exogenous variables that shape the 3SLS regression. Hundreds and forty-seven (147) samples were included with total 1323 observations from 1995 until 2003. Internal institutional ownership has the highest mean than other main variables. This result suggests that internal institutional ownership is the majority in Indonesia listed firms. Majority of the observation have negative free cash flow, and more than 50% debt ratio.

Table 1. Descriptive Statistics

Samples are 147 listed firms in Jakarta Stock Exchange from 1995 – 2003. Nine endogenous and exogenous variables will be included in Three Stage Least Square regression (including four control variables).

Variables	Mean	Standard Deviation	Standard Error of Mean
DEBT	0.631382	0.294969	0.008110
MOWN	0.006233	0.023872	0.000656
FCF	-0.387535	0.393609	0.010821
D	0.053666	0.225442	0.006198
INST	0.642958	0.201757	0.005547
Control Variables			
DCRISIS	0.666667	0.471583	0.012965
DIV	0.578231	0.494029	0.013582
SIZE	0.581672	0.537825	0.014786
ROA	0.016481	0.129043	0.003548

Note:
 DEBT = debt policy
 MOWN = managerial ownership
 FCF = free cash flow
 D = dummy for low and high growth firms
 INST = internal institutional ownership
 Control Variables:
 DCRISIS = dummy crisis period (D=0; 1995-1997, and D=1; after 1997)
 DIV = dividend policy
 SIZE = size of the firm
 ROA = return on assets

Table 2. Regression Result for 3SLS

Two equation are examine using 3SLS which much more powerfull than 2SLS. Identification problems were conduct and support the use of 3SLS.

Variables	Coefficient	t-Statistic
Equation 1: DEBT		
Coefficient	0.868888	24.32590 ***
FCF	0.008590	0.432512
FCF*D	-0.718154	-4.194948 ***
MOWN	-1.055258	-1.845578 *
INST	-0.075442	-1.817699 *
SIZE	-0.028828	-2.062239 **
DCRISIS	-0.017765	-0.923167
DIV	-0.272830	-15.31577 ***
R ²	15.5%	
Adjusted R ²	15%	
Equation 2: MOWN		
Coefficient	0.036208	11.01414 ***
DEBT	-0.006309	-2.454866 **
DIV	-0.003109	-1.895820 *
SIZE	-0.000353	-0.299297
DCRISIS	-0.004730	-2.986053 ***
ROA	-0.003932	-0.699362
INST	-0.032305	-10.26630 ***
R ²	8.5%	
Adjusted R ²	8.1%	

Significant level: ***) 1%; **) 5%; and *) 10%

This result also suggests that listed firms in Indonesian have small portions of share hold by managers. Internal institutional ownership on the other hand owned more than 50% of ownership. This result supports Mahadwartha (2004) that argues internal institutional ownership as majority

shareholders and hold superior control of manager's actions.

The Three Stage Least Square (3SLS) regression result will show in Table 2. Table 2 divides into two panels, which represent equation one and two for 3SLS.

Free cash flow have positive coefficient but insignificant. Hypothesis 1a (H1a) said that free cash flow would positively affect debt policy. High level of free cash flow will support managers' perquisites therefore; shareholders will bind the behavior using debt policy. Agency theory argues such activity as bonding mechanism on perquisites action. Debt will obligate firms (managers) to pay certain amount of their income for interest payment. The result shows practically significant positive relationship between free cash flow to debt policy but statistically insignificant.

The interaction coefficient is statistically significant and shows confirmation on hypothesis 1b (H1b). Firms with high growth level will have negative relationship on free cash flow to debt policy, but firms with low growth level will have positive relationship on free cash flow to debt policy. For high growth firm the coefficient is 0.00859 + (-0.718154) = -0.709564; which is confirm the hypothesis practically and statistically. Tabel 3 shows the differences of the coefficient between high and low growth firm on the relationship of free cash flow to debt policy. The Wald test shows significant result and support H1b hypothesis.

Table 3. Wald Test of Interaction Effect

Wald test implements to test the effect of growth level on the relationship between free cash flow to debt policy.

Null Hypothesis:	$C(FCF) = C(FCF) + C(FCF * D)$
Chi-square	17.59759 ***

C: coefficient
 Significant level: ***) 1%; **) 5%; and *) 10%

High growth firm will need more cash flow to finance their growth both internally (in case of high level of cash flow) or externally using debt (in case of low level of cash flow). This research argues that debt will be use as bonding if the level of growth is low, and there is enough cash flow to prevent from perquisites of managers.

The result also confirms the interdependence of managerial ownership and debt policy with negative sign therefore hypothesis 2 (H2) confirms balancing of agency theory. Firms concerns on the trade off to implement control mechanism through managerial ownership structure, and debt policy. The result also shows confirmation on balancing of agency theory from the relationship of internal institutional ownership to debt policy (H3), and internal institutional ownership to managerial ownership (H4). The coefficients for both relationships are negative

and statistically significant. The result support previous empirical research such as Mahadwartha (2003), Mahadwartha and Hartono (2002), Tandeliilin (2003), and Ismiyanti and Hanafi (2004).

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