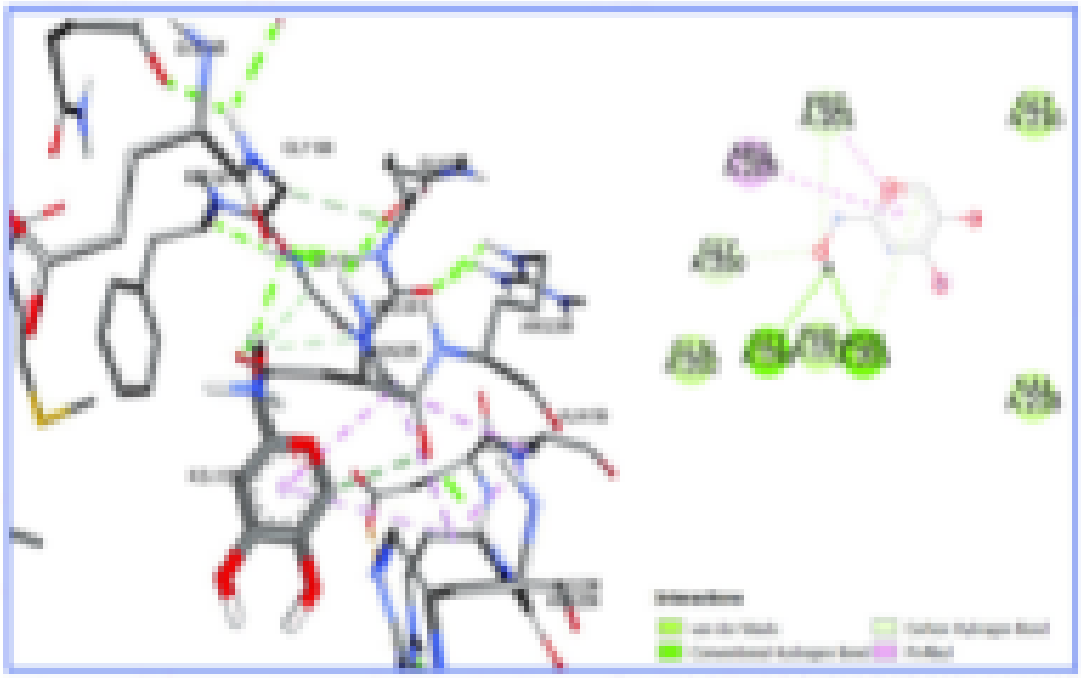
Volume 14 (Number 4) (OCT - DEC) (October - December) [2021]
www.rasayanjournal.com | www.rasayan.in

RASĀYAN
Journal of Chemistry

(An International Quarterly Research Journal of Chemical Sciences)



http://doi.org/10.31788/RJC.2021.1448418

Rasayan J. Chem.
ISSN (Print): 0974-1496
ISSN (Online): 0976-0083
CODEN: RJCABP

Abstracted in: Scopus, 2008

ELSEVIER
SCOPUS

Editorial Board

Editor-in-Chief:

Editorial Office:

CONTENTS

ARCHIVE ISSUES

DOWNLOADS

RJC CONFERENCE

SPECIAL ISSUES

Department of Chemical Engineering, School of Mining, Metallurgy and Chemical Engineering, University of Johannesburg, Doornfontein 2028, South Africa
Contact: +358400205215
Email: mikaesillanpaa@gmail.com
Research Interest: Water treatment

Pankaj KUMAR
Professor and Head, Department of Chemistry, University of Energy and Petrolium studies, Dehradun, India
Contact: +917351958165
Email: pkumar@ddn.upes.ac.in
Research Interest: Biofuels and Bioenergy, Chemical sensors, Nano-materials, Minimization of industrial wastes

R.V. SINGH
Ex Professor, Department iof Chemistry, University of Rajasthan, Jaipur,India
Contact: +91 941406975
Email: rvsjpr@hotmail.com
Research Interest: Inorganic Chemistry

Soro YAYA
Laboratoire des Procédés Industriels de Synthèse, de l'Environnement et des Energies Nouvelles (LAPISEN), Institut National Polytechnique (INP-HB),Yamoussoukro, BP 991 Yamoussoukro(Côte d'Ivoire)
Contact: (+225) 07 71 67 66
Email: soro_y@yahoo.fr
Research Interest: Organic synthesis, Natural Products, waste management

V.K. GARG
Professor and Dean Centre for Environmental Science and Technology School of Environment and Earth Sciences Central University of Punjab, Bathinda- 151001, India
Contact: +919812058109
Email: vinodkgarg@yahoo.com
Research Interest: Pollution Monitoring and abatement, Solid Waste Management, Radioecology

Professor, Department of Chemistry, Ahmadu Bello University, Zaria, Kaduna State, Nigeria
Contact: +2348038198753
Email: nabukeddy@yahoo.com
Research Interest: Physical Chemistry, Computational Chemistry, Nanochemistry, Industrial Chemistry, Environmental Chemistry

Priyan PERERA
Director - Center for Sustainability
Department of Forestry and Environmental Science
University of Sri Jayewardenepura, Sri Lanka
Contact: +94 718656457
Email: priyan@sjp.ac.lk
Research Interest: Environmental Sustain

Ramesh. L. GARDAS
Department of Chemistry Indian Institute of Technology Madras Chennai-600 036, India
Contact: +91 9884996125
Email: gardas@iitm.ac.in
Research Interest: Physical Chemistry, Chemical Thermodynamics, Alternative Solvents

Susheel MITTAL
Senior Professor, School of Chemistry & Biochemistry, Thapar Institute of Engineering & Technology (Deemed to be University), Bhadson Road, Patiala-147004, India
Contact: +91-9815653261
Email: smittal2001@yahoo.com
Research Interest: Voltammetric Sensors, Potentiometric Sensors, Biosensors, Ambient Air Quality and Human Health

Willian Aperador CHAPARRO
School of Engineering, Universidad Militar Nueva Granada, Bogotá-111121, Colombia
Contact: + 57 3142220552
Email: william.aperador@unimilitar.edu.co
Research Interest: Materials, batteries, corrosion, coatings, tribology

Important Links

Home
About us
Contact
Archive
Abstracted
Announcement
Editorial Board
Author's Guidelines
Subscription
Manuscript Submission
Current Issue

About Rasayan

Rasayan J. Chem.
ISSN: 0974-1496(Print)
ISSN: 0976-0083(Online)
CODEN: RJCABP
Frequency: March, June, September & December

Archive Issue

Volume 15, Number 1, 1-737, January- March (2022)

A REVIEW ON PHYTOCHEMICAL AND PHARMACOLOGICAL PROPERTIES OF Syzygium caryophyllatum

— Ramadevi Pemmereddy, K. S. Chandrashekar, Sreedhara Ranganath K. Pai, Vasudev Pai, Anna Mathew and B. Venkatesh Kamath

PHYTOCHEMICAL SCREENING AND MICROBIAL ASSESSMENT OF Moringa oleifera SEED CRUDE OIL EXTRACT

— M.E. Ojewumi, O.R. Obanla, S.O Taiwo and A.N. John

MOLECULAR DOCKING OF β-SITOSTEROL AND STIGMASTEROL ISOLATED FROM Morinda citrifolia WITH α^AMYLASE, α-GLUCOSIDASE, DIPEPTIDYLPEPTIDASE-IV, AND PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-γ

— N. Lolok, D. S. F. Ramadhan, S. A. Sumiwi, I. Sahidin and J. Levita

PHOTOCHEMICAL REDUCTION OF COPPER AND SILVER IONS ON CELLULOSE-CONTAINING FABRICS

— M.S. Sataev, Sh.T. Koshkarbaeva, K.B. Amanbaeva, P.A. Abdurazova, G.T.Assilbekova, Y.B. Raiymbekov and D.Urazkeldieva

SPECTRAL CHARACTERIZATION, DNA BINDING PROPERTIES AND ANTIBACTERIAL ACTIVITY OF NEW METALLO HYDRAZONES

— Y.B. Nagamani, K. Hussain Reddy, K. Srinivasulu, K. Anuja and D. Dhanalakshmi

THE EFFICACY OF GINGER ESSENTIAL OIL WITH CHITOSAN TO VIABILITY of Staphylococcus aureus IN FF

— Flora Elvistia Firdaus, Adam Saputra and Anisfa Neva Wardana

SYNERGISTIC CORROSION-WEAR EFFECT IN AUSTENITIC POWDER METALLURGICAL STEEL WITH DIFFEREN ADDITIONS

— W. Aperador, J. Bautista-Ruiz and J. Caicedo

SIMPLE HPLC METHOD FOR THE QUANTIFICATION OF GINGEROLS (4-, 6-, 8-, AND 10-) AND SHOGAOLS (6-, 8-, AND 10-) IN Zingiber officinale var. rubrum SUPERCRITICAL CARBON DIOXIDE (SC-CO2) EXTRACT

— Shiming Zhang, Kit-Kay Mak, Puvaneswari Marappan , Madhu Katyayani Balijepalli, Gun-Hean Chong and Mallikarjuna Rao Pichika

SYNTHESIS AND CHARACTERIZATION OF COPPER OXIDE NANOPARTICLES USING DIFFERENT PRECURSOR

— Jagdish Prasad, Vinod Kumar, Bhuwan Chandra and N.D. Kandpal

CONTENTS

CURRENT ISSUE *Online First*

ARCHIVE ISSUES

DOWNLOADS

RJC CONFERENCE

SPECIAL ISSUES *Announcement*

SCOPUS Indexed Since, 2008 & UGC Approved

2.1 CiteScore 2020
45th percentile
Powered by Scopus

SJR SCImago Journal & Country Rank
Rasayan Journal of Chemistry
Q2 Pharmacology, Toxicology and Pharmaceutics... best quartile
SJR 2021 0.33
powered by scimagojr.com

STRUCTURE CHARACTERIZATION OF STRESS DEGRADATION PRODUCTS OF ELAGOLIX BY USING HRMS, NMR

— S. S. K. Chakravarthy Kotha, K.V.K. Mohan P, Raju Doddipalla, Dasameswara Rao Kavitapu, Chidananda Swamy Rumalla, Himabindu Gandham, Muralidharan kaliyaperumal

PRECIPITATED CALCIUM CARBONATE (PCC) FROM CORAL REEF AS RAW MATERIAL FOR SYNTHESIS OF HYDROXYAPATITE NANOPARTICLES

— Y. Azis, N. Jamarun, C. D. Alfarisi, A. Mutamima, Komalasari, Nurfatihayati, and V. Sisca

SYNTHESIS OF BIOACTIVE MEMBRANES FOR GUIDED TISSUE REGENERATION (GTR): A COMPARATIVE STU EFFECT SILANE-BASED CROSS-LINKER

— Mahmudi, Nuryono, B. Pidhatika and Suyanta

CHARACTERISTICS OF CHARCOAL BRIQUETTES FROM KEPOK BANANA PEEL WASTE (Musa paradisiaca F.) AS ALTERNATIVE FUEL

— Supriadi, S. Rahmawati, P. H. Abram, Afadil, N.G.A.M. Parwati and Anggraini

ELECTROLYTE OPTIMIZATION ON DRY CELL GENERATOR ELECTROLYSIS SYSTEM FOR PRODUCING HYDROGEN GAS USING RSM METHOD (RESPONSE SURFACE METHOD)

— Rahadian Zainul, Efran Ustia Rahmad, Kawther Ameen Muhammed Saeed Aledresi, Wimbi Apriwanda Nursiwan, Guspatni, Siriboon Mukdasai and Riso Sari Mandeli

UTILIZATION OF ACTIVATED CARBON FROM CANDLENUT SHELLS (Aleurites Moluccana) AS METHYLENE BLUE ADSORBENT

— Buhani, S.N. Halimah, Suharso and Sumadi

In-vitro PHYSICOCHEMICAL PROPERTIES AND ANTIBACTERIAL ACTIVITY OF CIPROFLOXACINCARRAGEENAN INHALABLE MICROSPHERES

— D.M Hariyadi, E. Hendradi, M. Rahmadi, N.S. Bontong, E. Pudjadi and N. Islam

PLS CALCULATION OF FTIR AND SPECTROPHOTOMETRIC METHODS FOR DETERMINATION SIMULTANEOUS OF DEXTROMETHORPHAN HBR AND GLYCERYL GUAIACOLATE IN TABLET MIXTURE

— Muchlisyam Bachri, Yade M. Permata and H. Syahputra

ZINC COATINGS FROM ALKALINE ELECTROLYTES WITH SURFACTANTS

— N.A. Vysotskaya, B.N. Kabylbekova, G.M. Adyrbekova, A.S. Tukibayeva, R.S. Spabekova, A. Zh. SuigenbaÑfeva1 and L. D. Aikozova

SYNTHESIS, DOCKING AND BIOLOGICAL EVALUATION OF 3-(3-CHLOROBENZOYL)-N-PHENYLINDOLIZINE-1-CARBOXAMIDE DERIVATIVES AS ANTI-TUBERCULOSIS, ANTICANCER, ANTI-INFLAMMATORY AND ANTIBACTERIAL AGENTS

— G. Mahanthesha, T. Suresh and T.R. Ravikumar Naik

NOVEL QUINOXALINE DERIVATIVES: SYNTHESIS, THERMAL, PHOTO PHYSICAL STUDIES AND BIOLOGICAL ACTIVITY

— R. Raman, B. Natarajan and M. L. Sundararajan

IMPACT OF Mn2+ IONS ON MICRO-STRUCTURAL, LUMINESCENCE PROPERTIES OF ZnS-MoS2 NANOCOMPOSITES FOR OPTOELECTRONICS

— K. Venkatarao, G. Sreedevi , Y. Nirmal Rajeev, B. Tirumala Rao and Sandhya Cole

WOUND HEALING ACTIVITY OF PUNICALIN AND PUNICALAGIN ISOLATED FROM Punica granatum L.

— A. Kumar, R. Mishra, V. D. Singh, A. Mazumder, R. Mazumder and A. Kumar

THE INFLUENCE OF OLEIC ACID AND BENZOYL PEROXIDE AGAINST OLEIC ACID GRAFTED ONTO LLDPE

— A.H. Ritonga, N. Jamarun, S. Arief, H. Aziz, D.A. Tanjung and B. Isfa

SPECTROPHOTOMETRIC DETERMINATION OF IRON CONTENT IN SIX INDIGENOUS GREEN LEAFY VEGETABLES CONSUMED IN MUAK LEK, THAILAND

— Anthoney Swamy Thangiah, Aldrich Titus Anthoney and Wilai Laolee

ANALYSIS OF CRUDE RICIN FROM Ricinus communis ORIGINATED FROM NGANJUK, EAST JAVA, INDONESIA, USING LIQUID CHROMATOGRAPHY, COLUMN LIQUID CHROMATOGRAPHY, AND FAST PROTEIN LIQUID CHROMATOGRAPHY (FPLC)

— I. E. Herawati, R. Lesmana, I. Levita and A. Subarnas

MODIFICATION OF STRUCTURAL, THERMAL, ELECTRICAL AND DIELECTRIC PROPERTIES OF La0.7Sr0.3FexMn1-xO3 {x=0.2 AND 0.3} WITH Fe DOPING FOR CATHODE APPLICATION IN SOFCs

— Surinder Paul, Manokamna, Arun Kumar, D. K. Sharma, A. Singh and Arvind Kumar

NUCLEAR MAGNETIC RESONANCE (1HNMR) STUDY OF CHROMIUM (III) SALICYLATE AND BENZOATE COMPLEXES

— Manoj Kumar Mishra

REMOVAL OF METHANAL FROM AQUEOUS SOLUTION USING MICROWAVE INDUCED CARBON FROM Coffea arabica GROUNDS WASTE

— M. Nazar, N. M. Aulya, Syahrial and K. Puspita

BIOACTIVE COMPOUNDS OF INDONESIAN RED BETEL (PIPER CROCATUM) EXTRACT AND ITS INHIBITORY ACTIVITY IN MCF-7 CELL LINE

— K. Assidqi, N.F. Sianipar and R. Tarigan

PROXIMATE ANALYSIS, PHYTOCHEMICAL SCREENING, TOTAL PHENOLIC CONTENT AND In-Vitro ANTIOXIDANT POTENTIAL OF Prunus domestica L. (SEED COAT)

— Kishan, R. K. Shukla, A. Shukla and R. Singh

INFLUENCE OF SURFACTANTS ON THE SCATTERING ABILITY OF SULPHATE ELECTROLYTES OF CADMIUM PLATING AND THE QUALITY OF CADMIUM COATINGS

— N. A. Vysotskaya, B. N. Kabylbekova, A. S. Tukibayeva, L. D. Aikozova, M. M. Narmanov and S. S. Pernebekov

ACUTE TOXICITY AND ANTIFUNGAL ACTIVITY OF THE OINTMENT Murraya koenigii ETHANOL EXTRACT

— M. F. Lubis, V. E. Kaban, J. O. Aritonang, D.Satria , A. A. Mulina and H. Febriani

STUDIES ON THE LIQUID PHASE EXTRACTION AND SPECTROPHOTOMETRIC DETERMINATION OF 6-CHLORO3-HYDROXY-7-METHYL-2-(2'-FURYL) -4H-CHROMEN-4-ONE COMPLEX OF PALLADIUM(II)

— N. Kaur, R. Agnihotri and N. Agnihotri

ETHYL ACETATE FRACTION IN ETHANOL EXTRACT OF NONI FRUIT MODIFIED BY ZEOLITE AS ANTI-SEBORRHEIC DERMATITIS: In-vitro AND In-silico STUDIES

— L. Susanti, R. Mustarichie, E. Halimah and D. Kurnia

DEVELOPMENT AND VALIDATION OF STABILITY INDICATING ASSAY BY HPLC METHOD FOR THE ESTIMATION OF

DEVELOPMENT AND VALIDATION OF STABILITY INDICATING ASSAY RP-HPLC METHOD FOR THE ESTIMATION OF ANIDULAFUNGIN AND RELATED COMPOUNDS IN PARENTERAL DOSAGE FORM

— C. S. Tejasvini, S. Sekhar, R. Verma and L. Kumar

SYNTHESIS OF THIOESTERS AND THIOAMIDES USING POTASSIUM THIOCYANATE UNDER MICROWAVE IRRADIATION

— Deepika D., Santosh L. Gaonkar, Nitin Kumar S. Shetty

VISCOMETRIC STUDY ON BINARY LIQUID MIXTURES OF PROPIOPHENONE WITH ANILINE AND N-ALKYL SUBSTITUTED ANILINES, AT 303.15 TO 318.15 K

— Nanduri Gayatri Devi, N.V.N.B. Srinivasa Rao, D. Ramachandran, V. Nagalakshmi, and P. Sunila Rani

DESIGN AND SYNTHESIS OF NOVEL PERILLYL-4HPYRANTRIAZOLE DERIVATIVES

— Navaneetha Depa and Harikrishna Erothu

A NEW MICROWAVE-ASSISTED METHOD FOR THE SYNTHESIS OF 2-SUBSTITUTED-THIAZOL-4(5H)-ONE VIA HANTZSCH CONDENSATION

— Swarnagowri Nayak and Santosh L Gaonkar

DIFFRACTION AND MAGNETIZATION PROPERTIES OF Fe3O4 NANOPARTICLE FROM NATURAL IRON SAND IN VARIOUS STIRRING RATE FOR POTENTIAL BIOMEDICAL APPLICATIONS

— A.N. Syahida, H. Sutanto, M. Manawan, E. A. Setiadi, A. A. Wibowo, F. D. D. Irianti, I. Alkian ,E. Hidayanto, P. Priyono, I. Marhaendrajaya, and P. Triadyaksa

GREENER SYNTHESIS OF PYRANOPYRAZOLE DERIVATIVES CATALYZED BY CaO NANOPARTICLES

— Sangeeta, Har Lal Singh, Mamta Chahar, Saloni Sahal and Sarita Khaturia

A SIMPLE SENSITIVE AND RAPID GAS CHROMATOGRAPHY METHOD FOR DETECTION AND QUANTIZATION OF METFORMIN IN METFORMIN TABLET FORMULATION, BY DIRECT INJECTION, USING MASS DETECTOR

— M. D. Dâ€™Souza, P. Dwivedi, R. S. Lokhande, T. Anvekar, S. K. Sharma and A. J. Dâ€™Souza

SPATIAL DISTRIBUTION OF URANIUM IN GROUNDWATER AND ITS HEALTH RISK ASSESSMENT IN HARYANA, INDIA

— Naresh Tanwer, Pradeep Khyalia, Meena Deswal, J.S. Laura and Babita Khosla

ELECTROCHEMICAL STUDIES OF NITRO BENZOIC ACIDS AT DIFFERENT pH ON GLASSY CARBON AND STAINLESS STEEL (SS-316) ELECTRODE

— S. K. Sharma and A. Sharma

QSAR MODELING AND DESIGN OF A NEW MODEL OF ANTI-HIV DRUG 1-ARYL-TETRAHYDROISOQUINOLINE DERIVED USING THE PM3 SEMIEMPIRICAL METHOD

— Yusthinus T. Male, I. W. Sutapa, I. B. Kapelle and M. Lopulalan

C-PHYCOCYANIN FROM Spirulina platensis AS A SUBSTRATE CANDIDATE FOR PROTEASE ACTIVITY ASSAY OF PANCREATIN: ISOLATION, CHARACTERIZATION AND KINETIC ASSAY

— Tursino, E. Julianti, T. Gusdinar and S. Damayanti

ANTIPLASMODIAL ACTIVITY AND MALATE QUINONE OXIDOREDUCTASE INHIBITOR OF STEROID ISOLATED FROM Fibraurea tinctoria

— Riski Sulistiarini, Andreanus Andaja Soemardji, Elfahmi, Maria Immaculata Iwo, Dian Japany Puspitasari, Erwahyuni Endang Prabandari and Danang Waluyo

ANALYZING ANTIMICROBIAL ACTIVITY OF ALUMINIUM DOPED ZnO THIN FILMS

— BA. Anandh, R. Sakthivel, A. Shankar Ganesh, S. Subramani and A.T. Rajamanickam

SYNBIOTIC FUNCTIONAL DRINK FROM COW MILK FERMENTED WITH KEFIR AND SUPPLEMENTED WITH INULIN

— F. Sebayang, M. Z. E. Sinaga, A. Kahiri, J. B. Tariganand E. K. Sitepu

ANTIBACTERIAL PROPERTIES AND UV- PROTECTION OF COTTON FABRIC USING NANOHYBRID MULTILAYER ZnOSiO2/CHITOSAN AND DODECYLTRIETOXYSILANE (DTS)

— Yetria Rilda, Prima Vidya Puti Ayuni, Refinel Refinel, Armaini Armaini, Anthoni Agustien, Almurdi Almurdi and Hilfi Pardi

STOPPED FLOW KINETICS AND MECHANISTIC STUDY OF PERIODATE DEGRADATION OF PERSIST CARCINOGENIC 2,6 XYLIDINE BY Mn(II) CATALYST

— Karuna Saini, R. D. Kaushik and Jaspal Singh

GREEN SYNTHESIS OF REDUCED GRAPHENE OXIDE SILVER NANOCOMPOSITE USING Anisomeles malabarica (L.) R. BR. LEAF EXTRACT AND ITS ANTIBACTERIAL ACTIVITY

— R. Rakkimuthu, S. Aarthi, E. Neelamathi, P. Sathishkumar, A. M. Anandakumar and D. Sowmiya

WET CHEMICAL GROWTH OF ONE DIMENSIONAL ZnO FILM

— P. L. Meena, Yogesh Kumar, Pooja Bhardwaj, Mahaveer Genwa, Dinesh Kumar Arya, Asha Verma and Surinder P. Singh

STUDY OF ELECTRICAL PROPERTIES AND SOLVENT BEHAVIOUR OF 6-(4-CHLOROPHENYL)-1, 2, 3, 4- TETRAHYDRO-4-OXO-2-THIOXOPYRIMIDINE-5- CARBONITRILE AT DIFFERENT TEMPERATURES

— M. R. Gaware

THE NiO AND MoO3 ENRICHED ZSM-5 AS CATALYST FOR THE HYDROCRACKING OF COCONUT OIL INTO BIO-JET FRACTION

— Sriatun, A. Darmawan, H. Susanto and Widayat

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF 4-THIAZOLIDINONE AND ITS DERIVATIVES BASED ON ISONIAZID

— Hiteshkumar Gujjar, Sheetal Gulati, H. S. Patel and Hitesh Samata

SYTHESIS OF RUTHENIUM(II) COMPLEXES WITH CARBOXAMIDE DERIVATIVES: SPECTROSCOPIC CHARACTERISATION AND STUDIES ON DNA AND BSA INTERACTION

— Hena Paul, Rajesh Chakraborty and Pabitra Chattopadhyay

ANALGESIC AND ANTI-INFLAMMATORY ACTIVITIES OF NOVEL HETEROCYCLIC SUBSTITUTED THIAZOLE DERIVATIVES

— Neeharika Yamsani and Raja Sundararajan

HYDROGEN PEROXIDE TREATED IRON OXIDE IMPREGNATED CARBON MATERIALS FOR IMPROVED ADSORPTION AND PHOTOCATALYTIC DEGRADATION OF CATIONIC DYES

— A. Edwin Vasu and A. P. Mary Sri Archana

DOCKING STUDIES AND SYNTHESIS OF NOVEL 4- THIAZOLIDINONE DERIVATIVES BEARING 1, 3, 4- OXADIAZOLE MOIETY AS SIRT-3 ACTIVATORS TARGETING PARKINSON'S DISEASE

— Gomathy Subramanian, Farhath Sherin, Naina Merin Joy, Ashish D Wadhwani, Gowramma Byran and A Shanish Antony

In-silico DESIGN SCREENING OF SOME PYRAZOLONE FUSED HETEROCYCLIC ANALOGUES AS HER2 INHIBITORS TARGETING BREAST CANCER

— A. Sumathy, R. Suresh and N. L. Gowrishankar

PLANT MEDIATED GREEN AND FACILE SYNTHESIS OF SILVER NANOPARTICLES AND THEIR POSSIBLE APPLICATION AS ANTIMICROBIAL AGENTS

— A. D. Dhimdhime, R. S. Talegaonkar, A.K.Wanjari, A. R. Somwanshi and R. D. Ghodile

MULTIFUNCTIONAL CrxCa(10-x)Al30Si60 GLASSES, ELECTRICAL CONDUCTIVITY AND THERMOLUMINESCENCE

— Kodumuri Veerabhadra Rao, Padala Ashok and B. Appa Rao

EFFECT OF IONIC STRENGTH ON MORPHOLOGICAL CHARACTERISTIC AND THE STABILITY OF Ag/ALGINATE NANOPARTICLES: THEORETICAL REVIEW BASED ON THE ENERGY OF PARTICLE FORMATION

— Foliatini and Nurdiani

REUSE OF WASTE CRAB SHELLS FOR SYNTHESIS OF CALCIUM CARBONATE AS A CANDIDATE BIOMATERIAL

— A.P. Bayuseno, A.I. Prasetya, R. Ismail, B. Setiyana and J.Jamari

THE ANTIOXIDANT ACTIVITIES OF ACID HYDROLYSIS OF κ-Carrageenan

— A. W. M. Diah , M. F. Raihan, S. Rahmawati, P. Ningsih, Afadil, S. Nuryanti and Supriadi

BIO-UTILIZATION OF INDUSTRIAL WASTE: CHARACTERIZATION AND ANTIOXIDANT ACTIVITY

— P. Jindal and M. S. Chauhan

THE PORE FORMATION AND DOPING PROCESS ON THE SYNTHESIS OF NITROGEN-DOPED TITANIA THROUGH SOL-GEL METHOD

— C. Kusumawardani

ISOLATION OF THE ACTIVE COMPOUND FROM THE BARK OF Cinnamomum burmanniiAS A SUNSCREEN

— R. Nasution, D. Mailidar, M. Bahi, N. Saidi, M. Marianne and M. Iqhrammullah

SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF PYRAZOLE-PYRIMIDONE CLUBBED DERIVATIVES

— Nikulsinh Sarvaiya, Hitesh Samata, Sheetal Gulati, and H. Patel

TiO2-Ag AND NATURAL DYE CO-PIGMENTED WITH SALICYLIC ACID FOR DYE-SENSITIZED SOLAR CELL (DSSC) APPLICATION

— Hardeli, H. Sanjaya, P. Permatasari, I. P. Novita, N. F. Agdisti, R. Luli and L. Yunita

COMPARATIVE STUDY OF Co/MESOPOROUS SILICA AND Co-NH2/MESOPOROUS SILICA CATALYSTS ACTIVITY IN WASTE COCONUT OIL HYDROCRACKING

— Wega Trisunaryanti, Triyono, Nugroho Raka Santoso, and Dyah Ayu Fatmawati

ANALYSIS OF THE ENRICHMENT PROCESS OF NATURAL POTASSIUM SALTS

— Galina Seitmagzimova, Aigerim Assylkhankyzy, Almagul Kadyrbaeva and Roza Abisheva

EVALUATION OF DAIRY EFFLUENT DETOXIFICATION AND REMOVAL EFFICIENCY IN AN INTEGRATED WASTEWATER TREATMENT SYSTEM USING LOW-COST ADSORBENTS

— R. S. Rajput, M. Singh, P. Kumar and N. K. Srivastava

COLORIMETRIC METHOD FOR TOTAL PHENOLIC AND FLAVONOID CONTENT DETERMINATION OF FIG (Ficus carica L.) LEAVES EXTRACT FROM WEST JAVA, INDONESIA

— N.M. Saptarini, R. Pratiwi and I.T. Maisyarah

INFLUENCE OF SUB-CHRONIC EXPOSURE TO ARSENIC, CADMIUM, LEAD ON GROWTH AND ACCUMULATION OF ITS IN Oreochromis sp.

— Nguyen Quoc Thang, Le Van Tan and Nguyen Thi Kim Phuong

ELECTROCHEMICAL SYNTHESIS OF ZINC CHELATES IN NON-AQUEOUS MEDIA

— D. D. Asylbekova, M. Zh. Duisembiyev, N.N. Issabayev, G.F. Sagitova,A. Zh. Suigenbayeva, A. E. Bitemirova and A. S. Abdibek

USING PREPARATIVE CHROMATOGRAPHY AND NMR/LCMS/FT-IR, ISOLATION, IDENTIFICATION, AND CHARACTERIZATION OF POSACONAZOLE OXIDATIVE DEGRADATION IMPURITIES

— Naga Venkata Durga Prasad Ketha and Deepti Kolli

SYNTHESIS AND SPECTRAL STUDIES OF HETEROBIMETALLIC SCHIFF BASE COMPLEXES

— Sachin Prakash, Anju Kumari Gupta, Shivani Prakash, K.R.R.P. Singh and D. Prakash

In-vitro AND In-silico STUDIES OF AYURVEDIC MEDICINAL PLANTS PIPALI AND JYOTISHMATI FOR AChE INHIBITION: APPROACH FOR TREATMENT OF MEMORY DISORDER

— Vasudev Pai, M. Manjunath Setty, Aravind Pai, Anuraag Muralidharan, and K. S. Chandrashekar

COMPARATIVE STUDY OF Sida rhombifolia FROM TWO DIFFERENT LOCATIONS

— E. R. Laili, N. S. Aminah, A. N. Kristanti, A. P. Wardana, M. Rafi, A. Rohman, M. Insanu and K. N. W. Tun

FABRICATION AND STRUCTURAL CHARACTERIZATION OF SrSiO3/TiO2 PHOTOCATALYST FOR THE DEGRADATION OF CONGO RED DYE UNDER SUNLIGHT

— Preeja P. Thattil and A. Leema Rose

EFFECT OF SUBSTRATE CONCENTRATION AND FeCl2 ADDITION ON L-ASPARAGINASE ACTIVITIES OF BACTERIA SYMBIONTS BROWN ALGAE Sargassum sp. AND ITS POTENTIAL AS A NEW ANTI-DENGUE AGENTS

— A. Ahmad, N. Asmi, H. Karim, M. N. Massi and I. Wahid

MICROWAVE ASSISTED ONE-POT THREE-COMPONENT SYNTHESIS OF 3,4-DIHYDROPYRIMIDIN-2(1H)-ONES USING SFHS AS AN EFFICIENT AND REUSABLE CATALYST

— A.S. Waghmare, K.R. Kadam, V.D. Murade and S.S. Pandit

PHYTOCHEMICAL SCREENING, CYTOTOXIC ACTIVITY AND MOLECULAR DOCKING STUDIES OF Eclipta alba LEAVES EXTRACT AGAINST ORAL CANCER

— Lavanya Jayaraman, Subhashini Shivaji and Shanmugam Anandakumar

MOLECULAR FIELD-BASED QSAR STUDIES AND DOCKING ANALYSIS OF MERCAPTOQUINAZOLINONE BENZENE SULFONAMIDE DERIVATIVES AGAINST hCA XII

— P. Gopinath and M. K. Kathiravan

GLYCOSYLATED FLAVONOID COMPOUND FROM COCOA PARASITE LEAVES (Dendrophthoe pentandra (L.) Mig.)

— H. Br. Sembiring, L. Marpaung, M. Basyuni and P. Simanjuntak

PHYTOCHEMICALS, ANTIOXIDANT ACTIVITIES, AND TOXICITY EVALUATION OF SEVERAL FRACTIONS OF Scorodocarpus borneensis Becc. LEAVES

— Y. S. K. Dewi, S. Purwayantie, F. Christian, D. Fadly and C.J.K. Simamora

DESIGN, In-silico STUDIES, SYNTHESIS, CHARACTERIZATION, AND ANTICONVULSANT ACTIVITIES OF NOVEL THIAZOLE SUBSTITUTED OXAZOLE DERIVATIVES

— Singagari Srilakshmi and Raja Sundararajan

DESIGN AND SYNTHESIS OF NOVEL 1,2,3–TRIAZOLE SCAFFOLDS: BIOLOGICAL ACTIVITY AND MOLECULAR DOCKING STUDIES

— Ganji Sreekanth Reddy, Venkateswara Rao Anna, Saikrishna Balabadra and I.V. Kasi Viswanath

Important Links

Home
About us
Contact
Archive
Abstracted
Announcement
Editorial Board
Author's Guidelines
Subscription
Manuscript Submission
Current Issue

About Rasayan

Rasayan J. Chem.
ISSN: 0974-1496(Print)
ISSN: 0976-0083(Online)
CODEN: RJCABP
Frequency: March, June, September & December

RJC

RASĀYAN *J. Chem.*
Vol. 15 | No. 1 |132-142| January - March | 2022
ISSN: 0974-1496 | e-ISSN: 0976-0083 | CODEN: RJCABP
http://www.rasayanjournal.com
http://www.rasayanjournal.co.in

In-vitro PHYSICOCHEMICAL PROPERTIES AND ANTIBACTERIAL ACTIVITY OF CIPROFLOXACIN-CARRAGEENAN INHALABLE MICROSPHERES

D.M Hariyadi[1,✉], E. Hendradi[1], M. Rahmadi[2], N.S. Bontong[1,3], E. Pudjadi[4] and N. Islam[5,6]

[1]Pharmaceutical Sciences Department, Faculty of Pharmacy, Universitas Airlangga, Campus C Jl. Mulyorejo 60115, Surabaya, Indonesia
[2]Clinical Pharmacy Department, Faculty of Pharmacy, Universitas Airlangga, Campus C Jl. Mulyorejo 60115, Surabaya, Indonesia
[3]Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Tadulako University, Palu, Indonesia
[4]Center for Safety and Radiation Metrology Technology (PTKMR)-National Nuclear Energy Agency of Indonesia (BATAN)
[5]Queensland University of Technology, School of Clinical Sciences, Brisbane, Australia
[6]Institute of Health and Biomedical Innovation (IHBI), Queensland University of Technology, Brisbane, QLD, Australia
✉Corresponding Author: dewi-m-h@ff.unair.ac.id

ABSTRACT

This study's aim is to characterize aerosolization properties of ciprofloxacin loaded kappa-carrageenan microspheres for pulmonary delivery. Ciprofloxacin-carrageenan microspheres by ionotropic gelation were prepared and characterized for moisture content, yield, drug loading, efficiency, aerosolization properties, activity and stability. Characteristics showed spherical microspheres, smooth and size below 2µm, moisture content of <4%, yield of 46-58%, encapsulation efficiency of 40-94% and loadings of 25-37%. Optimum microspheres containing 1%w/v carrageenan and 0.6% w/v KCl, showed 58% yield, 38% loading 94.5% efficiency with slowest release. The fine particle fraction was 30%. The increased concentration of polymers from 0.5% to 1% and crosslinker from 0.2% to 0.6% significantly increased moisture content, yield, drug loading, efficiency, and aerosolization. Ciprofloxacin-carrageenan microspheres were found to be stable up to 30 days storage and have high activity against Staphylococcus aureus and Pseudomonas aeruginosa at a low dose. Inhaled ciprofloxacin-carrageenan microspheres may be useful against respiratory tract infection.

Keywords: Ciprofloxacin HCl, Kappa Carrageenan, Inhalable Microspheres, Release, Stability, Respiratory Infectious Diseases.

RASĀYAN *J. Chem.*, Vol. 15, No.1, 2022

INTRODUCTION

Ciprofloxacin HCl is a broad-spectrum fluoroquinolone antibiotic that inhibits the DNA-girase and topoisomerase IV present in bacterial cells that are responsible for the reproduction of bacterial DNA.[1] The inhaled liposomal ciprofloxacin showed a dual release of the drug with potent antipseudomonal efficacy in adults with non-cystic fibrosis (CF) bronchiectasis.[2] When compared to the systemic route of antibiotics, the inhaled antibiotic was found to be optimized on the target site and pharmacokinetic/pharmacodynamics aspects to reduce toxicity.[3,4] Around 70% of the Ciprofloxacin HCl is absorbed after oral administration.[5] Around 15% of the drug is metabolized by the liver enzyme and 40-50% is excreted through urine.[6] Ciprofloxacin as an inhalation dosage form has advantages such as the faster onset of action and smaller doses compared to those of intravenous and oral preparations.[7] Lung drug delivery avoids first-pass metabolism and ensures limited systemic side-effects compared with oral dosages forms.

Carrageenan, a sulfated polygalactan, is biodegradable and widely used for drug encapsulation[8,9], has been used to produce ciprofloxacin encapsulation cross-linked with potassium chloride (KCl). KCl can form transparent and stable gel besides has elasticity and cohesivity.[8] Stability studies were carried out to ensure product quality, safety, and efficacy during the shelf life of the product. Exposure to temperature, humidity and light are highly influenced stability. The purpose of this research is to study the characteristics, activity and stability of Ciprofloxacin-loaded carragenan microspheres for dry powder inhaler formulation. The stability study was based on the International Council on Harmonization guidelines. Using an Andersen Cascade Impactor (ACI), the in-vitro dispersibility of the prepared powders was carried out. Optimum microspheres define as microspheres that have a particle size less than 5µm, high encapsulation efficiency, yield, drug loading and slower release to fulfill pulmonary delivery system.

EXPERIMENTAL

Materials

Ciprofloxacin HCl pharmaceutical grade (Zhejiang Ltd., China), Kappa-Carrageenan Nusantara pharmaceutical grade (KCN, Pasuruan, Indonesia), KCl pharmaceutical grade (New Jersey, USA), Maltodextrin pharmaceutical grade (Zhucheng Ltd., Shandong, China), Aqua destilata (Bratachem, Indonesia).

Microspheres Formulation

Solutions of Ciprofloxacin HCl, Kappa Carrageenan and KCl were separately prepared. A mixture of ciprofloxacin and KCl were prepared and sprayed into the Carrageenan solution. The sprayed distance is 8 cm and the spray nozzle diameter is 35 µm. Solutions were aerosolized (40 psi). The solution was stirred at 1000 rpm for 2 hours and separated using a centrifuge at 1000rpm for 10 minutes (Eppendorf centrifuge, Germany) and filtered to separate the particles. The obtained wet particles were freeze-dried for 48 hours at -50°C.[10,11] Wet microspheres were added by maltodextrin (5% w/v of microspheres) as lyoprotectant during the freeze-drying process. Maltodextrin can stabilize the microspheres from the pressure during the process. Schematic of microspheres formulation and formulas of microspheres are shown in Fig.-1 and Table-1.

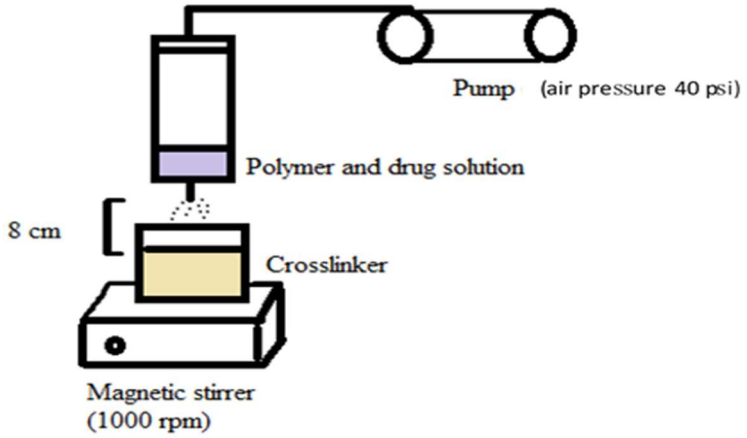


Fig.-1: Schematic of Microspheres Formulation

Table-1: Ciprofloxacin-Carragenan Microspheres Formula

Formula	Ciprofloxacin (%w/v)	Carrageenan (%w/v)	KCl (%w/v)	Maltodextrin (%w/v)
F1	1	0.5	0.2	5
F2	1	0.5	0.4	5
F3	1	0.5	0.6	5
F4	1	1	0.2	5
F5	1	1	0.4	5
F6	1	1	0.6	5

FTIR Spectra Analysis

The FTIR spectra of all formulations were obtained using FT-IR (Perkin Elmer Instrument) spectrophotometer. The FTIR band spectra were examined to investigate the structural integrity in different formulations. The spectra were collected after scan for 4000–500 cm^{-1} wavenumber to investigate the observed fingerprint of ciprofloxacin (O–H, C=O, COOH, C=C and C–F) and carragenan bands (S=O, C–H, C–O–C, O–H, and galactose sulphate) relating to the region of ciprofloxacin (3200-3400 cm^{-1}, 1600-1700 cm^{-1}, 1700 cm^{-1}, 1250-1300 cm^{-1}, 1300 cm^{-1}) and carrageenan's region (1100-1200 cm^{-1}, 3400 cm^{-1}, 800-1200 cm^{-1}, 2800-2900 cm^{-1} and 840-850 cm^{-1}) that has often been investigated by the researchers.[12-15] The carragenan have wide and strong absorption bands in 1100-1000 cm^{-1} region, which are typical of polysaccharides with the sulphate stretching bands occurring at around region 850 $cm^{-1,}$ mainly for carrageenan.

Differential Scanning Calorimetry (DSC)

Using a DSC TGA (Mettler Toledo FP 85, Switzerland), the thermal properties of all formulations were determined. Samples about 5mg of all formulas were scanned (from 30°C to 250°C) with a heating rate of 10°C/min. The characteristic of prominent DSC peak, which represents endothermic peak showed by temperature, was determined.

Scanning Electron Microscopy (SEM)

Morphology was evaluated by SEM. The sample was mounted, coated for 120 seconds and was then examined with an SEM microscope (HITACHI FLEXSEM 100, Japan) at a working distance of 10 mm, with 20 kV beam energy.

Particle Size by Optical Microscope

Microspheres of 300 particles were determined using optical microscope Optilab and Image Raster Software. The average diameter was calculated using the equation:

Diameter average = "Σnd" /"Σn" (1)

n = number of microspheres observed

d = size of the microspheres

Yield

The yield was calculated according to the total recoverable final weight of microparticles to evaluate efficiency in producing microspheres. The yield was calculated using equation[16]:

% Yield = (Weight of dry microspheres)/ (Total weight material (polymer and drug)) x 100% (2)

Drug Loading

The ciprofloxacin loading in carrageenan was determined using a UV-Vis spectrophotometer. A 50 mg microsphere was added to Phosphate Buffer Saline, which has pH of 7.4, and was stirred for 24 hours at 1000rpm. The solution was filtered, and the absorbance was measured at a wavelength of 268 nm (taken from in-house validation). The amount of the drug was determined using a validated in-house standard calibrated plot. The drug loading was calculated using equation the equation below:

Drug loading = (Weight of drug)/ (Weight of microspheres) x 100% (3)

Entrapment Efficiency

Entrapment efficiency was calculated using equation below[17]:

Entrapment efficiency = (Drug content in microspehers)/(Theoritical drug content in formula) x 100% (4)

Drug Release

Ciprofloxacin release from the microspheres was tested in phosphate-buffered saline (PBS) at a pH level of 7.4. The released test was carried out using a Thermo shaker at 37ºC with 100 rpm. 400 mg of microspheres were added to 100 ml PBS solution (pH 7.4) on a Thermo shaker at 37 ± 0.5 °C and stirred

at 100 rpm. Samples (5 ml) were taken for drug analysis. Samples were taken after 15, 30, 60, 90, 120, 180, 240, 300, 360, 420, 480, 540, 600, 660, 720, 780 and 840 minutes. During each sampling time, the media was replaced. Samples were filtered using Millipore filter paper 0.45 µm. Using a UV-Vis spectrophotometer, the amount of ciprofloxacin HCl was determined at a wavelength of 276 nm.

Stability Test

The accelerated stability testing was carried out on the ciprofloxacin-carragenan microspheres. The microspheres were poured into a vial and stored in a room 25 ± 2˚C and 40 ± 2˚C, RH 75 ± 5% for 30 days. The stability of the prepared formulations was tested by organoleptic property, morphology, drug loading, and particle size. These parameters were according to Li and Gong's method (2016).[18]

Bulk Density

Bulk density was determined by the ratio of powder weight compared to initial volume (100 mL cup full of powder) of the untapped powder (powder without compaction) as below equation:

Bulk density = (powder weight (gram))/(Initial volume of powder(ml)) (5)

Tapped Density

Tapped density was determined by filling the material into a 100 mL volume measuring cup, after tapping 500 times using a motorized tapping device, and the final volume of powder was measured:

Tapped density= (powder weight (gram))/ (volume after tapping (ml)) (6)

Hausner Ratio and Carr's Index [11,19]

Carr's Index= (tapped density - bulk density)/ (tapped density) (7)

Hausner Ratio = (tapped density)/ (bulk density) (8)

***In-vitro* Aerosolization Study**

Using an Andersen Cascade Impactor (ACI), the aerosolization efficiency of the microspheres was carried out. A total of eight Mylar filters were stored for 24 hours in a desiccator and then weighed. ACI consists of stages (levels) 0, 1, 2, 3, 4, 5, 6, 7, and F. Cascade impactor connected with a flow meter and suction pump (generated by electricity), where the flow meter is set at 28.3 L/min.[20] A 50 mg of microspheres poured into the capsule shell (number 2) and filled into a DPI device (Handihaler®), then vacuumed by pulling air for 10 seconds at a flow rate of 28.3 L/min. The eight stages and filter container plates of the cascade impactor were washed, sonicated for 20 minutes, and then dried at 100°C using an oven for 60 minutes. The dispersibility of the formulation was named as aerodynamic criteria, including fine particle fraction (FPF), recovered dose (RD) and emitted dose (ED)[21]. The fine particle dose (FPD) as the dose of the aerosolized drug particles with an aerodynamic diameter < 5µm was determined. Fine particle fraction (FPF) was the ratio of FPD to the total recovered dose (RD). The RD was the amount of drug transferred from the Handihaler® and the compartments. The ED is the total amount of drug emitted from the inhaler device.

Antibacterial Activity

Antibacterial activity against *Staphylococcus aureus* and *Pseudomonas aeruginosa* was carried out using a good diffusion technique. The bacterial inoculum was prepared using bacterial culture stock that was suspended in 0.9% NaCl. The inoculum was then measured for transmittance at the wavelength of 580 nm by a UV-Vis spectrophotometer. Transmission suspension was set to reach 25%. A 50 grams of each microspheres were suspended into 100 ml phosphate-buffered saline at pH 7.4 ± 0.05 for the antimicrobial test. Standard solution of Ciprofloxacin HCl (0.02%) as the positive control, PBS solution as negative control and blank microspheres were also prepared.

For media preparation, the base layer (30mL) and the seat layer media (20mL) were filled with nutrient agar (NA) solution. The medium was then sterilized for 30 minutes at 121˚C. The base layer media of 30 mL was poured into a petri dish and was allowed to cool and solidify. The seat layer media was added onto the solidified media with 8µL inoculum bacterial suspension. The seat layer media consisting of inoculum was added into the solid base layer media, and again it was allowed to cool and solidify.

After it had cooled and solidified, the wells on the agar plate were made and were sterilized. The same distance between the measured holes was maintained. Positive and negative controls, blank microspheres and all formula microspheres suspensions (20µL) were poured into each well. All Petri dishes were incubated for 24 hours at 32.5°C. The diameter of zone inhibition was observed and measured.

Data Analysis

All data are presented in mean ± SD. One-way analysis of variance and post hoc Tukey's were used for antibacterial activity analyses. $p<0.05$ was considered to be statistically significant. Data are triplicated n = 3.

RESULTS AND DISCUSSION

Characterization of Microspheres

This study investigated the effect of the concentrations of κ-carrageenan polymer and KCl on the formation and physical characterization of microspheres produced by ionotropic gelation. Maltodextrin in the freeze-drying process replaced water molecules by forming hydrogen bonds between maltodextrin and polar groups on the surface of the microspheres during the drying process. Therefore, the smooth microspheres were protected and prevented from aggregation.[22] Results of characterization by FTIR spectra and analysis of F1 to F6 were presented in Table-2. The functional groups of ciprofloxacin HCl, kappa-carragenan, microspheres and the possibility of presence or shifting of the wavenumbers were studied. Referring to the ciprofloxacin compound, the wavenumber of the characteristic peak of amide band vibration N-H, COOH stretching, C-H stretching, C = C aromatic and C-F stretching was present in all formulas of microspheres indicated the stability of ciprofloxacin in the microspheres. For formulations F1 to F6, the shift of wavenumber of the amide band of ciprofloxacin HCl was from 1624.15 cm^{-1} to between 1625.56 cm^{-1} and 1630.44 cm^{-1}. The wave shift in κ-carrageenan occurred in the ester sulphate group (S = O) from 1160.9 cm^{-1} to between 1155.42 and 1192.70 cm^{-1}; the methyl group (C-H) from wavenumber 3435.7 cm^{-1} to between 3405.55 and 3429.60 cm^{-1} and the loss of the C-O-C group. These indicated that there were interactions between the κ-carrageenan polymers and crosslinker to form microspheres. FTIR of KCL and maltodextrin cryoprotectant were not shown in this paper. Importantly, the functional group of galactose sulphate, which was specific for kappa carrageenan, also shifted from wavenumber 848.68 cm^{-1} to between 845.67 and 845.80 cm^{-1}. Interactions between the polymer and the crosslinker and the existence of the ciprofloxacin drug indicated that new microspheres were formed and showed that the structural integrity of the materials was stable and maintained; this was also confirmed by other researchers.[23,24]

Table-2: FTIR of All Microspheres Formulas

Functional groups	Wave Number (cm-1)							
	Ciprofloxacin HCl	k-Carrageenan	F1	F2	F3	F4	F5	F6
O-H stretching	3205.47	2924.61	2926.70	2926.68	2926.68	2924.65	2927.51	2924.61
COOH stretching	1707.14	1717.65	1713.74	1710.74	1709.68	1708.59	1712.52	1717.65
N-H vibration	1624.15	1630.61	1630.69	1630.68	1627.65	1625.56	1630.44	1630.61
C-H stretching	1494.18	1493.64	1494.72	1492.71	1494.67	1495.59	1494.47	1493.64
Aromatic C=C	1272.17	1384.64	1384.72	1384.70	1384.69	1384.65	1384.49	1384.64
C-F stretching	1384.34	1274.63	1274.69	1273.68	1273.65	1273.58	1273.43	1274.63
C-O-C	1263.70	1028.58	1077.64	1079.61	1192.70	1025.62	1077.38	1263.70
S=O	1160.90	1189.65	1155.67	1155.64	1155.67	1192.70	1155.42	1160.90
C-H	3435.70	3423.52	3429.60	3422.56	3428.59	3405.55	3418.36	3435.70
O-H	2963.30	2924.61	2926.70	2926.68	2926.68	2924.65	2927.51	2963.30
Galactose sulphate	845.68	845.80	845.75	845.67	845.71	845.72	845.67	845.68

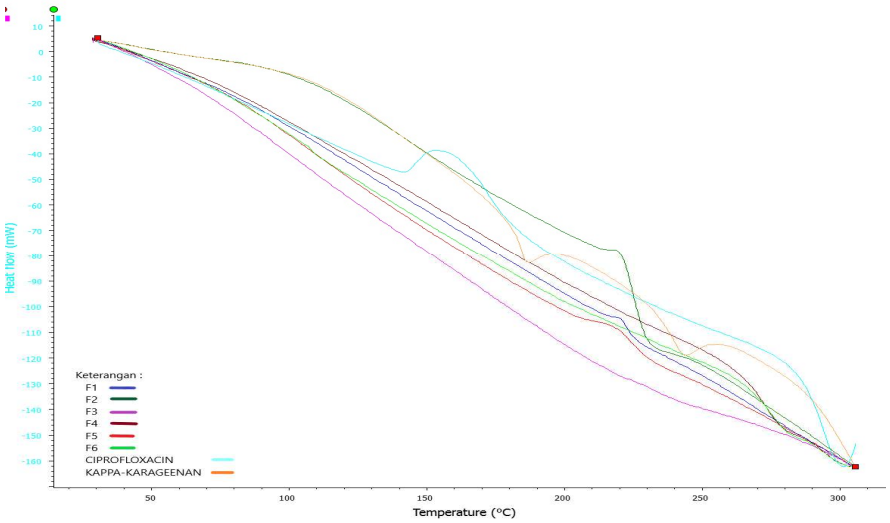


Fig.-2: DSC of all Formulas and Compounds of Ciprofloxacin and Carragenan

DSC results of all formulas are shown in Fig.-2. From DSC results, the endothermic peak of Ciprofloxacin HCl was at 180.2 °C and a second peak at 298.7 °C. Kappa-Carrageenan showed a prominent characteristic endothermic peak at 186.5 °C and 243.2 °C. All of these DSC peaks of ciprofloxacin HCl of 180.2 °C and 298.7 °C were disappeared in the microspheres formulation, which indicated an interaction between the drug, lyoprotectant maltodextrin, crosslinker, and polymer. DSC thermogram of lyoprotectant was not shown in this paper. All the microspheres (F1 to F6) were found to demonstrate the presence of endothermic peaks in the range between 186.5 ˚C and 298.7˚C. This indicated an interaction occurred and can confirm that the stable microspheres were completely formed by crosslinking. In addition, Kappa-Carrageenan showed an endothermic transition above 100 °C. This may indicate a hydrophilic nature of Carrageenan polymer, which was similar to the findings by other researchers.[9, 25]

Results of physical characteristics of the microspheres in this study were discussed as follows. Figure-3 shows the scanning electron microscopy of all six formulas. The moisture content test showed the lowest moisture content in F1 (1.90%), and the highest was F6 (3.79%) (Table-3). This was in agreement with the specification of kappa-carrageenan according to the Certificate of Analyze (CoA) (less than 12%). Morphology of the ciprofloxacin-kappa carrageenan microspheres of all formulas, F1 to F6, was a smooth spherical shape (Fig.-3). The particle size of F1 to F6 had a size less than 2µm; therefore, these particles are of an inhalable size and can be deposited in alveoli.[26]

In terms of yield (Table-4), F1 had the lowest yield (46.88%), and the highest was F6 (58.40%). These results indicated that the ionotropic gelation method was a potential method in producing ciprofloxacin-kappa carrageenan microspheres. The lowest drug loading was F1 (25.36%), and the highest was F6 (37.40%). The lowest entrapment efficiency was F1 (40.42%), and the highest was F6 (94.49%). These results indicated that an increased polymer and KCL concentration affected EE and DL. This was because an increased concentration of polymer affected the capabilities of the polymer chain to crosslink stronger to increase the number of binding networks between each polymer. Therefore the system can bind the drug, increasing the entrapment efficiency and drug loading efficiency.[27-28]

Drug Release

The cumulative drug release profile showed the highest release of the drug (96.08% ± 15.93) from the formulation F1, which demonstrated a faster release profile.The slowest drug release of 75.46% ± 12.95 (Fig.-4) was obtained from the formulation F6. The higher the concentration of the polymer, the slower the release of the drug because a higher polymer concentration increased the thickness layer around the drug particles and caused a slower drug diffusion from the matrix because the surface of the microspheres was coated with a polymer.[28-29] The release kinetics showed the ciprofloxacin-kappa carragenan

microspheres followed the Higuchi model. These results were similar to the outcome of other researchers who demonstrated the matrix models of drug release from microspheres following the Higuchi model (Table-5).[19] The drug release mechanism from this polymer matrix system involves the swelling of microspheres followed by diffusion and release of the drug by dissolution and subsequent diffusion.[30-31]

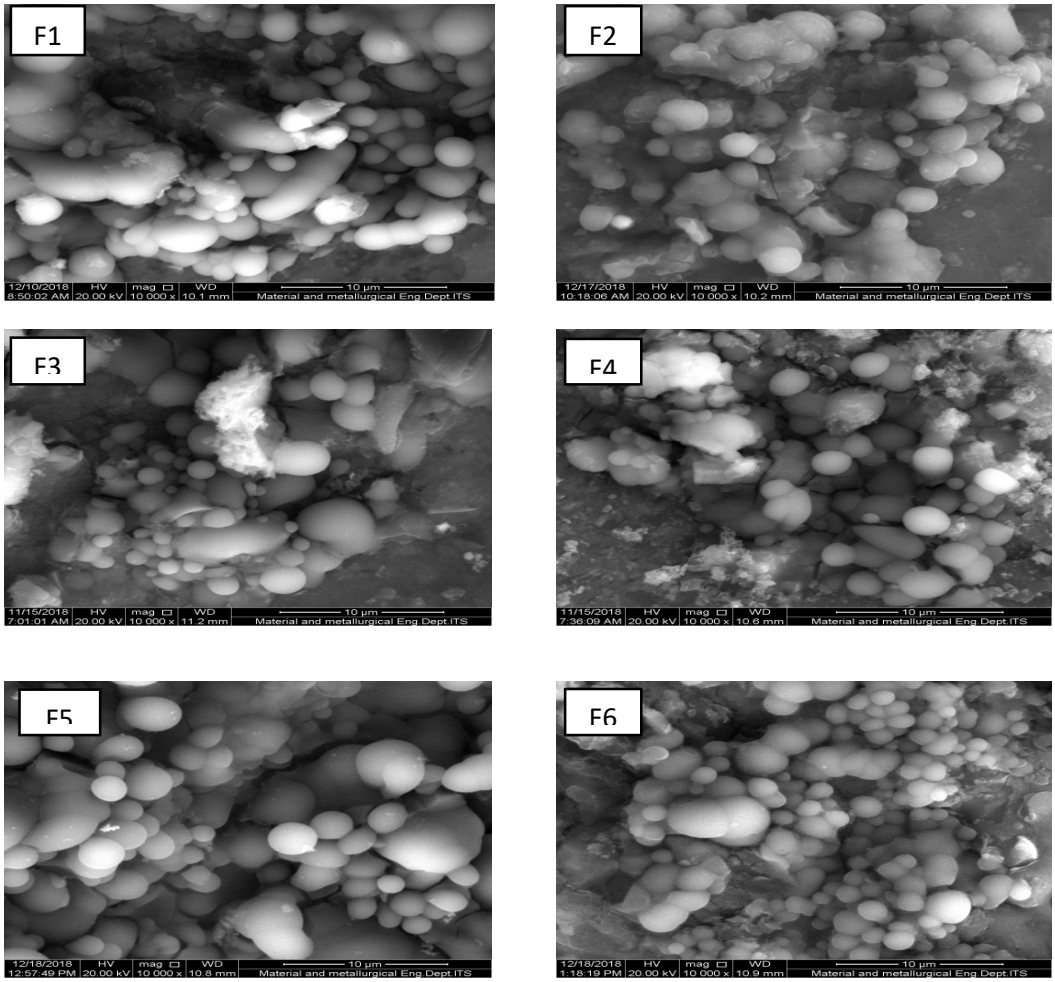


Fig.-3: SEM Images of Microspheres F1, F2, F3, F4, F5 and F6 (at 10000x)

Table-3: Moisture Content and Particle Size of Ciprofloxacin-kappa Carrageenan Microspheres

Formula	Moisture Content (%w/w)	Particle Size (µm)
F1	1.91 ± 0.58	1.508 ± 0.191
F2	1.92 ± 0.72	1.531 ± 0.130
F3	1.99 ± 0.53	1.498 ± 0.112
F4	3.15 ± 0.37	1.347 ± 0.129
F5	3.50 ± 0.19	1.438 ± 0.219
F6	3.79 ± 0.10	1.504 ± 0.191

Table-4: DL, Yield and EE of Ciprofloxacin-kappa Carrageenan Microspheres

Formula	Yield (%w/w)	Drug Loading (%w/w)	Entrapment Efficiency (%w/w)
F1	46.88 ± 2.76	25.36 ± 4.09	40.42 ± 11.82
F2	48.90 ± 2.23	26.55 ± 4.92	48.26 ± 15.74
F3	50.79 ± 0.51	27.15 ± 4.68	58.26 ± 15.27
F4	53.44 ± 2.42	28.41 ± 4.48	78.94 ± 5.96
F5	55.62 ± 2.52	29.66 ± 3.84	83.83 ± 6.99
F6	58.40 ± 1.56	37.40 ± 1.68	94.49 ± 1.54

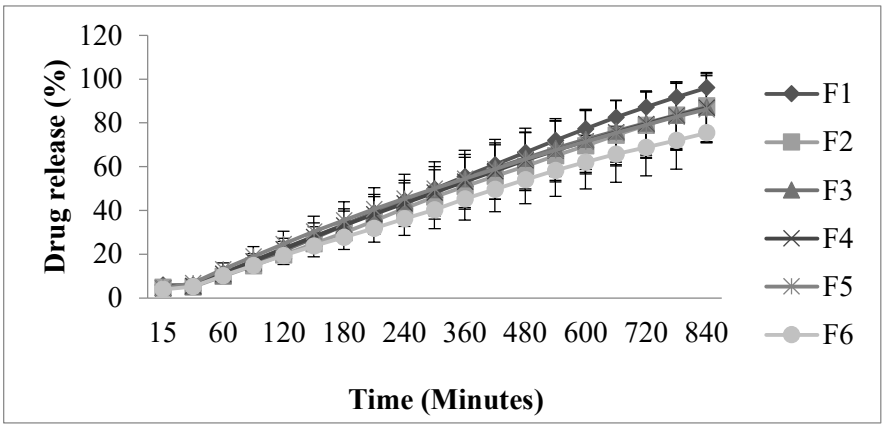


Fig.-4: Cumulative release of Ciprofloxacin from Kappa Carrageenan Microspheres

Table-5: Regression Coefficients of release Data by Curve fitting Method on Zero Order, First-order, Higuchi and Korsmeyer-Peppas

Formula	Order 0	Order 1	Higuchi	Korsmeyer-Peppas
F1	0.9740	0.7707	0.9940	0.9846
F2	0.9718	0.7617	0.9929	0.9839
F3	0.9522	0.7190	0.9937	0.9802
F4	0.9580	0.7244	0.9960	0.9857
F5	0.9471	0.9649	0.9961	0.9163
F6	0.9663	0.7393	0.9969	0.9937

Stability Studies

Results of the stability test at 25°C and 40°C after storage in 30 days in terms of particle size are presented in Table 6 and drug loading in figure 5. Organoleptic observations of all formulas did not show any changes, the color was still yellowish and did not aggregate. The microspheres' morphology was spherical with a smooth surface. Particle sizes of all formulations showed a small size of below 2 µm in all testing conditions (day 0 and after 30 days at 25 °C and 40 °C). No significant differences between the effect of temperature and time on drug loading and particle size were observed, which indicated that the ciprofloxacin-kappa carrageenan microspheres remained stable. To determine the possibility of the instability of microspheres, it takes a longer time and higher temperature to observe a significant difference in the physical stability of the ciprofloxacin-kappa carrageenan microspheres.

The most important parameter of dry powder inhalation is its flow properties and in vitro aerosolization. The result of powder flow properties is presented in Table-7. Flow properties which were indicated by the parameter of the Carr's index were <15%, and the Hausner ratio was <1.18. The result of F1 to F4 microspheres formulas had a Carr's index of 11-15% and a Hausner ratio of 1.12-1.18, including in the flow category "Good". In comparison, F5 and F6 had a Carr's Index <10% and a Hausner ratio of 1.00 - 1.11 as the category "Excellent". The final volume of F5 and F6 was reduced more than of F1-F4 after tapping. This phenomenon was because F5 and F6 had a greater density than F1 to F4 in accordance with other research that increases of polymers and crosslinker resulted in higher density[11]. From the results, it can be seen that ciprofloxacin - kappa carrageenan microspheres can produce sufficient flow property to be used for inhalation purposes.[29]

Table-6: The particle Size of Ciprofloxacin-Kappa Carrageenan Microspheres after 30 Days

Formula	Particle Size (µm)		
	0 Days	30 Days (25ºC)	30 Days (40ºC)
F1	1.615 ± 0.191	1.648 ± 0.126	1.721 ± 0.102
F2	1.564 ± 0.130	1.639 ± 0.113	1.673 ± 0.065
F3	1.495 ± 0.112	1.671 ± 0.093	1.793 ± 0.054
F4	1.347 ± 0.129	1.528 ± 0.069	1.633 ± 0.058
F5	1.437 ± 0.219	1.651 ± 0.213	1.663 ± 0.079
F6	1.504 ± 0.191	1.612 ± 0.187	1.501 ± 0.068

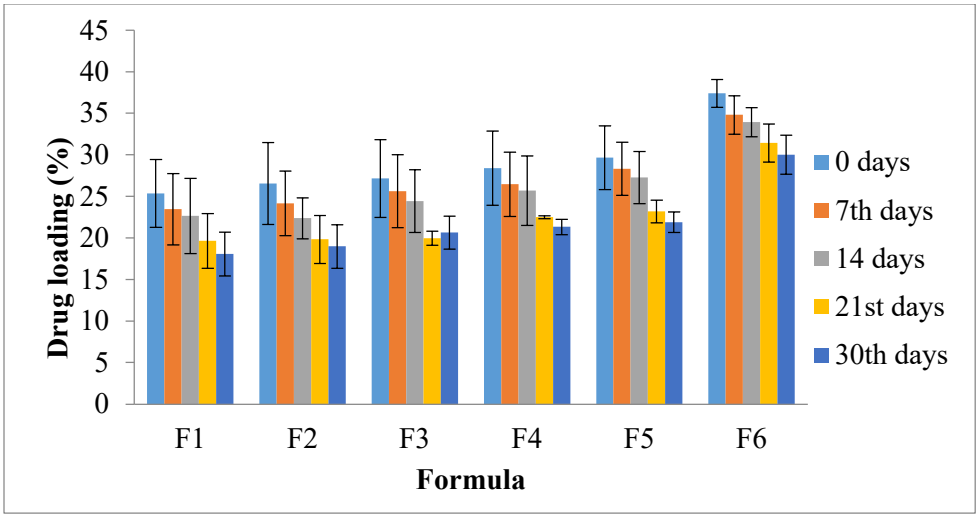


Fig.-5: Drug Loading of Ciprofloxacin-Kappa Carrageenan Microspheres after Storage for 30 Days at 40°C.

Table-7: Flow Properties Ciprofloxacin-Kappa carrageenan

Formula	Bulk Density	Tapped Density	Carr's Index (%)	Haustner Ratio
F1	0.021 ± 0.02	0.024 ± 0.02	12.62 ± 1.92	1.144 ± 0.025
F2	0.022 ± 0.02	0.025 ± 0.02	12.85 ± 1.30	1.147 ± 0.017
F3	0.021 ± 0.03	0.025 ± 0.04	11.18 ± 3.54	1.111 ± 0.068
F4	0.024 ± 0.03	0.027 ± 0.04	11.54 ± 2.14	1.131 ± 0.027
F5	0.026 ± 0.03	0.028 ± 0.04	9.10 ± 0.41	1.096 ± 0.012
F6	0.024 ± 0.03	0.027 ± 0.03	7.29 ± 2.94	1.096 ± 0.014

Aerosolization Study

Results of the in vitro aerosolization study to understand lung deposition using ACI are presented in Table-8. The percentage of the mass of the drug is at the stage of 0 to stage 3, which described the upper respiratory tract area showed all particles were found within the ideal DPI formulation range of less than 5 µm. As can be seen, the formulation F4 showed the highest FPF (33.6%), which has higher encapsulation efficiency. The formulation F6 showed the second highest FPF (28.2%). Therefore, considering its potential for efficiently inhalable particles, F4 and F6 could be selected as the optimized formula for inhalation.

Table-8: RD, ED and FPD of Ciprofloxacin-Kappa Carrageenan Microspheres

Formula	Recovered Dose (%)	Emitted Dose (%)	Fine Particle Fraction (FPF) (%)	Fine Particle Dose (FPD) (mg)
F1	39.2 ± 2.9	4.5 ± 0.6	24.1 ± 5.4	0.24 ± 0.05
F2	33.2 ± 1.0	5.9 ± 0.3	29.6 ± 4.8	0.29 ± 0.02
F3	62.8 ± 2.1	2.9 ± 0.4	14.0 ± 8.5	0.14 ± 0.08
F4	26.1 ± 1.6	7.1 ± 0.4	33.6 ± 4.4	0.34 ± 0.04
F5	46.7 ± 1.4	3.1 ± 0.2	12.1 ± 8.3	0.12 ± 0.08
F6	33.5 ± 1.4	8.1 ± 1.1	28.2 ± 4.2	0.28 ± 0.02

The low RD might be because of the increased moisture content of powder and produced aggregates, which did not reach the desired stage 3-7. DPI needs the energy to move powder to follow breathing airflow and break down the powder agglomerates into small isolated particles. The inhalation flow rate used in this study is 28.3L/min. The flow of inhalation is within the range of clinically effective flow rates for inhalers being tested and in accordance with industry standards for quality control of inhaled drugs[32]. Therefore, this study concluded that the optimized microsphere formula was F4 and F6.

Antibacterial Tests

The antibacterial activities of the prepared formulations against *Staphylococcus aureus* and *Pseudomonas aeruginosa* are presented in Table-9. F6 microspheres resulted in the highest activity against *Staphylococcus aureus* with equal activity compared to the positive control, whereas the F4 microsphere was the most active against Pseudomona-s aeruginosa. This might be due to the two highest FPD (F4 and

F6 of 0.34mg and 0.28mg, respectively) from where most particles were deposited in the target site producing higher antibacterial activity.

Table-9: *In-vitro* Antibacterial Activity of Microspheres against *Staphylococcus aureus* and *Pseudomonas aeruginosa*

Sample	Zone Inhibition Diameter (mm) against *Staphylococcus aureus*	Zone Inhibition Diameter (mm) against *Pseudomonas aeruginosa*
F1	12.70 ± 2.10	21.33 ± 1.53
F2	14.87 ± 1.54	17.33 ± 0.58
F3	14.93 ± 0.72	16.33 ± 0.58
F4	16.67 ± 0.50	24.67 ± 1.15
F5	18.45 ± 0.51	20.33 ± 0.58
F6	19.25 ± 0.15	15.20 ± 0.20
Positive Control (+)	22.00 ± 0.53	11.67 ± 0.58
Negative Control (-)	6.50 ± 0.50	6.00 ± 0.30

Data are presented as mean ± SD, n = 3. *The mean difference between formulas was significant at $p < 0.05$.

Moreover, based on the results of the antibacterial study, the concentration of ciprofloxacin HCl, which produce antibacterial activity in the F1 to F6 microspheres formula, the obtained data for fine particle dose (FPD) of F1, F2, F3, F4, F5 and F6 was of 0.24mg; 0.29mg; 0.14mg; 0.34mg; 0.12mg; and 0.28mg respectively. This FPD of microspheres produced antibacterial activity as high as ciprofloxacin HCl control. For the highest FPD of the formula, F4 and F6 were found to be almost 10 times lower compared to the oral pharmacokinetic dose for ciprofloxacin tablet as anti-infective, which is about 2.7mg[33]. It can be seen that the dose required for this current inhalable microsphere was smaller than the oral dose of ciprofloxacin per day. Thus, it can be recommended for the use of ciprofloxacin inhalable microspheres powder and further in vivo study was also highly recommended.

CONCLUSION

This study demonstrated the potential of Ciprofloxacin HCl-Kappa Carrageenan microspheres using 0.55 to 1.0% w/v carrageenan polymers and 0.2% to 0.6% w/v of potassium chloride for inhaled DPI formulation. Increasing the concentration of carrageenan polymers and KCl crosslinker increased the size, yield, EE and DL. The outcomes of Ciprofloxacin-carrageenan microspheres revealed the efficient dispersibility of the DPI formulations. The developed formulations produced good physical characteristics, good stability and high activities against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, which are the causative microbes for respiratory tract infections. Further study of in vivo activity is recommended to observe clinical applications of microspheres to measure the effectivity of the prepared formulations for lung delivery.

ACKNOWLEDGEMENT

The authors would like to thank the Directorate of Higher Education and Universitas Airlangga for all the support for this research under a grant of Penelitian Dasar by DRPM DIKTI No. 621/UN3.14/LT/2019.

REFERENCES

1. S. Naveed and N. Waheed. *Mintage Journal of Pharmaceutical and Medical Sciences,* **14(30)**, 10(2014).
2. D.J. Serisier, D. Bilton, A. De Soyza, P.J. Thompson, J. Kolbe, H.W. Greville. *Thorax,* **68**, 812(2013), https://doi.org/10.1136/thoraxjnl-2013-203207
3. E. Wenzler, R. Dustin, Fraidenburg, T. Scardina, L.H. Danziger. *Clinical Microbiology Reviews,* **229(3)**, 581(2016), https://doi.org/10.1128/CMR.00101-15
4. V. K. Jyothirmai, S.M.R. Sharmila and S. Arun, Rasayan Journal of Chemistry, **13(4)**, 2274(2020), http://dx.doi.org/10.31788/RJC.2020.1346074
5. M.M. Patel, U.H. Shah, K. Goswami, S. Bhavsar and S.G. Patel, *Rasayan Journal of Chemistry*, **13(4)**, 2361(2020), https://doi.org/10.31788/RJC.2020.1345941
6. Bayer Health Care Pharmaceuticals Inc. *Ciprofloxacin Hydrochloride (Tablets and Oral Suspension)*, (2008).

7. S. Shaikh, S. Nazim, T. Khan, A. Shaikh, M. Zameeruddin, A. Quazi. *International Journal of Applied Pharmaceutics,* **2(4)**, 27(2010).
8. A. Tecante, M.C.N. Santiago, *In Tech,* (2012), https://doi.org/10.5772/36619
9. E. Dzhakipbekov, S. Sakibayeva, N. Dzhakipbekova, B. Tarlanova, G. Sagitova and Z. Shingisbayeva, *Rasayan Journal of Chemistry*, **13(3)**, 1417(2020), http://dx.doi.org/10.31788/RJC.2020.1325709
10. D.M. Hariyadi, T. Purwanti, S. Adilla. *Journal of Pharmacy and Pharmacognosy Research,* **6(4)**, 250(2018).
11. D.M. Hariyadi, E. Hendradi, O.L.V. Piaya, C.N. Ramadani, *Pharma Scientia,* **2(1)**, 22(2013).
12. N. Rajasulochana, S. Gunasekaran, *Asian Journal of Chemistry,* **21(6)**, 4547(2009).
13. N. Devi, T.K. Maji. *Drug Development and Industrial Pharmacy,* **36(1)**, 56(2010), https://doi.org/10.3109/03639040903061355
14. B. Bhongade, S. Talath, S. Dhaneshwar. *International Journal of Spectroscopy,* **294612**, 1(2014), https://doi.org/10.1155/2014/294612
15. G.R. Mahdavinia, M.H. Karimi, M. Soltaniniya, B. Massoumi. *International Journal of Biological Macromolecules,* **126**, 443(2019), https://doi.org/10.1016/j.ijbiomac.2018.12.240
16. S. Hardenia, A. Jain, R. Patel, A. Kaushal. *Journal of Advanced Pharmacy Education & Research,* **1(4),** 214(2011).
17. C.R. Dhakar, D.S. Maurya, P.B. Sagar, S. Bhagat, K.S. Prajapati, P.C. Jain, *Der Pharmacia Lettre,* **2(5)**, 102(2010).
18. D. Li and L. Gong. *Drug Design Development and Therapy,* **10,** 2815(2016), https://doi.org/10.2147/DDDT.S113670
19. D. Durgapal, S. Mukhopadhyay, L. Goswami. *International Journal of Applied Pharmaceutics,* **9(1),** 1(2017), https://doi.org/10.22159/ijap.2017v9i1.14183
20. E. Pudjadi, B. Prayitno, S. Wahyuningsih, *URANIA,* **15(2)**, 61(2009).
21. M. A. Rashid, A. A. Elgied, Y. Alhamhoom, E. Chan, L. Rintoul, A. Allahham, N. Islam. *Pharmaceutics,* **11(207)**, 1(2019), https://doi.org/10.3390/pharmaceutics11050207
22. W. Abdelwahed, G. Degobert, S. Stainmess, H. Fessi. *Advanced Drug Delivery Reviews,* **58(15)**, 1688(2006), https://doi.org/10.1016/j.addr.2006.09.017
23. S. Kirubanandan, V. Subha, S. Renganathan. *Asian Journal of Pharmaceutics,* **11(2)**, 147(2017).
24. J. Singh, A. Jangra, J. Kumar, K. Rani and R. Kumar, Rasayan Journal of Chemistry, **13(1)**, 105(2020), http://dx.doi.org/10.31788/RJC.2020.1315382
25. S. Distantina, Rochmadi, M. Fahrurrozi, Wiratni. *Engineering Journal,* **17(3)**, 57(2013), https://doi.org/10.4186/ej.2013.17.3.57
26. K.A. Ashish, H.S. Chaudhari, P.L. Ughade, D.T. Baviskar, D.K. Jain. *International Journal of PharmTech Research,* **4(1)**, 293(2012).
27. S.G. Nanakia, G. Kyzas, A. Tzeremec, M. Papageorgiouc, M. Kostoglou, D.N. Bikiaris D.A. Lambropoulou. *Colloid Surface B: Biointerfaces,* **127**, 256(2015), https://doi.org/10.1016/j.colsurfb.2015.01.053
28. S. Joshi, P. Patel, S. Lin, P.L. Mada. *Asian Journal of Pharmaceutics,* **7(2)**, 134(2005).
29. A. Zafar, A. Bhattacharyya, M. Bajpai, M. Yasir, M. Asif. *International Journal of Pharmaceutical Sciences and Nanotechnology,* **7(1)**, 2356(2014), https://doi.org/10.37285/ijpsn.2014.7.1.7
30. F.M. Carbinatto, A.D. Castro, R.C. Evangelista, B.S.F. Cury. *Asian Journal of Pharmaceutical Sciences,* **9**, 27(2014), https://doi.org/10.1016/j.ajps.2013.12.002
31. S.A. Agnihotri, N.N. Mallikarjuna, T.M. Aminabhavi. *Journal of Controlled Release,* **100**, 5(2004), https://doi.org/10.1016/j.jconrel.2004.08.010
32. B. Johal, M. Howald, M. Fischer, J. Marshall, G. Venthoye, *Combination Products in Therapy,* **3**, 39(2013), https://doi.org/10.1007/s13556-013-0003-9
33. J.T. Lettieri, M.C. Rogge, I. Kaiser, R.M. Echols and A.H. Heller, *Antimicrobial Agents Chemotherapy,* **36**, 993(1992), https://doi.org/10.1128/AAC.36.5.993

[RJC-6652/2021]

Rasayan Journal of Chemistry

COUNTRY

India

Universities and research institutions in India

SUBJECT AREA AND CATEGORY

Biochemistry, Genetics and Molecular Biology
- Biochemistry

Chemical Engineering
- Chemical Engineering (miscellaneous)

Chemistry
- Chemistry (miscellaneous)

Energy
- Energy (miscellaneous)

Pharmacology, Toxicology and Pharmaceutics
- Pharmacology, Toxicology and Pharmaceutics (miscellaneous)

PUBLISHER

Rasayan Journal

H-INDEX

24

PUBLICATION TYPE

Journals

ISSN

09741496, 09760083

COVERAGE

2008-2021

INFORMATION

Homepage

How to publish in this journal

SCOPE

RASĀYAN Journal of Chemistry (RJC) signifies a confluence of diverse streams of Chemistry to stir up the cerebral powers of its contributors and readers. By introducing the journal by this name, we humbly intend to provide an open platform to all researchers, academicians and readers to showcase their ideas and research findings among the people of their fraternity and to share their vast repository of knowledge and information. The journal seeks to embody the spirit of inquiry and innovation to augment the richness of existing chemistry literature and theories. We also aim towards making this journal an unparalleled reservoir of information and in process aspire to inculcate and expand the research aptitude. RASĀYAN Journal of Chemistry (RJC) widely covers all branches of Chemistry including: Organic, Inorganic, Physical, Analytical, Biological, Pharmaceutical, Industrial, Environmental, Agricultural & Soil, Petroleum, Polymers, Nanotechnology, Green Chemistry, Forensic, Phytochemistry, Synthetic Drugs, Computational, as well as Chemical Physics and Chemical Engineering.

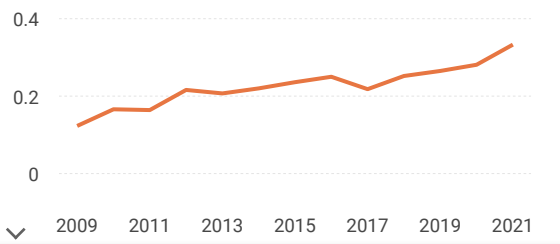
Join the conversation about this journal

Quartiles

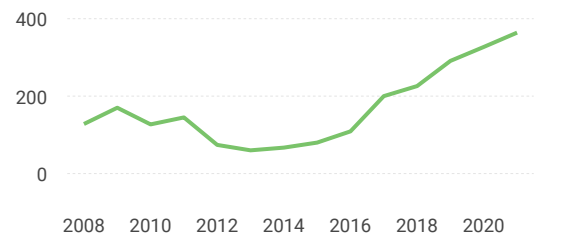
FIND SIMILAR JOURNALS

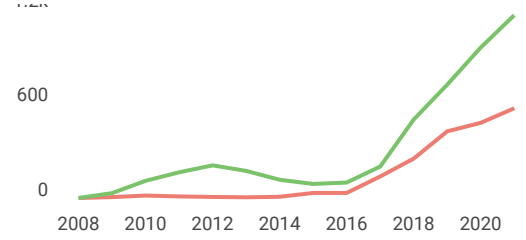
1	2	3	4
Asian Journal of Chemistry	**Oriental Journal of Chemistry**	**Arabian Journal of Chemistry**	**Mediterrane Chemistry**
IND	IND	SAU	MAR
16% similarity	16% similarity	16% similarity	1 s

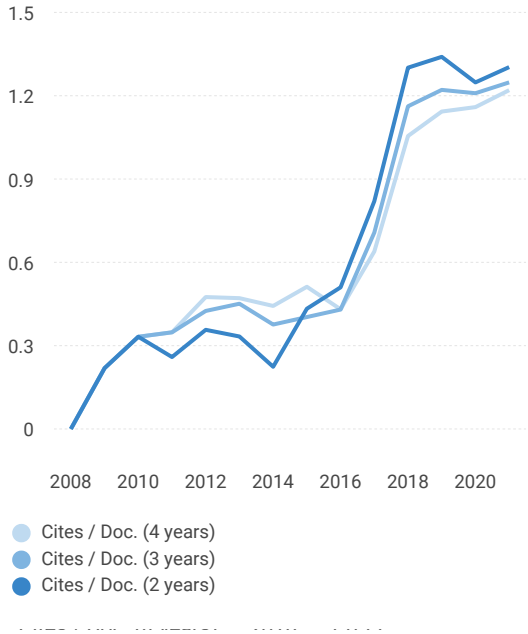
SJR



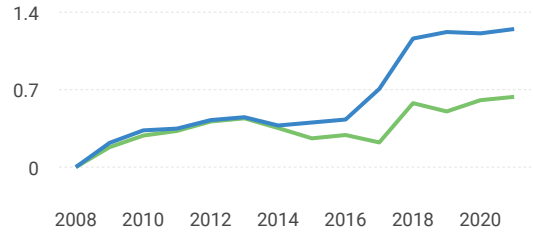
Total Documents



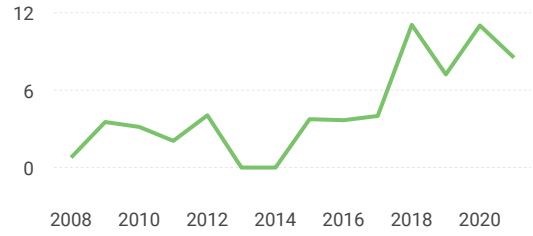




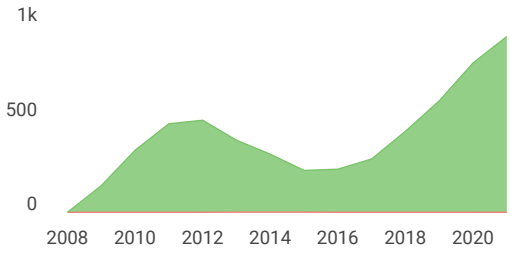
External Cites per Doc Cites per Doc



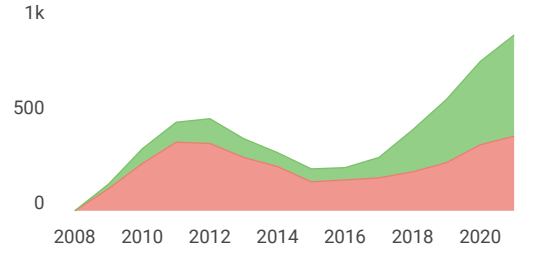
% International Collaboration

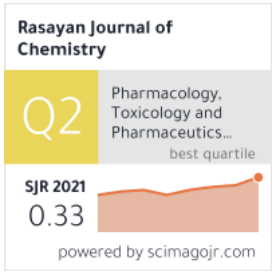


Citable documents Non-citable documents



Cited documents Uncited documents





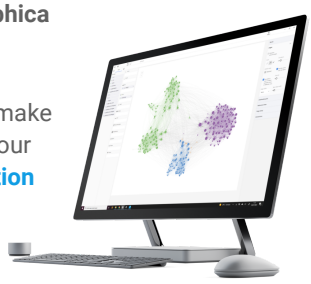
← Show this widget in your own website

Just copy the code below and paste within your html code:

<a href="https://www.scimag

SCImago Graphica

Explore, visually communicate and make sense of data with our **new data visualization tool**.



Metrics based on Scopus® data as of April 2022

Developed by: SCImago

Powered by: Scopus

Follow us on @ScimagoJR

EST MODUS IN REBUS
Horatio (Satire 1,1,106)

Edit Cookie Consent