RINGKASAN

PENGEMBANGAN SEDIAAN LEPAS LAMBAT NATRIUM DIKLOFENAK BERBASIS MATRIK ETILSELULOSA – PVP K 30

Untuk mengurangi efek samping yang terjadi karena penggunaan Na diklofenak, telah dikembangkan bentuk sediaan lepas lambat dari Na diklofenak. Selain dapat mengurangi efek samping, bentuk sediaan lepas lambat dari Na diklofenak juga dapat mengurangi frekuensi penggunaan, mengurangi fluktuasi kadar obat dan secara umum dapat meningkatkan kenyamanan pasien.

Pada penggunaan etilselulosa sebagai matrik lepas lambat Na diklofenak, dengan cara pencampuran fisik secara langsung didapatkan penghambatan hanya sekitar 2 jam. Hal ini karena matrik mengalami erosi dengan cepat saat uji disolusi sehingga pelepasan ND juga berjalan daaengan cepat.Untuk mengurangi erosi yang cepat dari matrik, dalam penelitian ini dikembangkan kombinasi antara etilselulosa dengan polivinilpirolidon (PVP) K-30. PVP K-30 dapat meningkatkan kekerasan tablet matrik sehingga menurunkan porositas matrik dan dalam media disolusi akan mengembang dan membentuk lapisan viskos sehingga proses erosi matrik berjalan dengan lambat, begitu pula pelepasan Na diklofenak dari matrik.

Mula – mula dibuat formula Na diklofenak – etilselulosa dengan perbandingan 1:2, 1:3 dan 1:4 (F1, F2, F3). Dari formula tersebut dibuat granul dengan pelarut etanol 96 % dan dikeringkan dalam lemari pengering pada suhu 50^0 C selama 2 jam. Granul diayak dengan pengayak mesh 20 dan ditampung dengan pengayak mesh 80. Granul yang tertampung dalam pengayak mesh 20 kemudian ditambah Mg Stearat 1 % dan dicetak menjadi tablet matrik dengan dosis Na diklofenak 100 mg. Tablet matrik diuji pelepasan Na diklofenaknya secara *in vitro* dengan uji disolusi menggunakan media disolusi dapar fosfat pH 6,8.

Dari uji pelepasan F1, F2 dan F3 didapatkan bahwa F2 yang paling sesuai untuk dikembangkan sebagai sediaan lepas lambat dengan penambahan PVP K-30. Kemudian F2 ditambah dengan PVP K-30 dengan persentase yang berbeda (5%, 10 % dan 15 % terhadap etilselulosa) sebagai F4, F5 dan F6.

Pada formula F4, F5 dan F6 dilakukan granulasi dengan metode yang sama seperti pada F1, F2 dan F3. Tablet matrik yang terbentuk diuji kekerasan dan kerapuhannya. Didapatkan kekerasan untuk tablet matrik F4, F5 dan F6 berturut – turut adalah 20,51±0,87 kp; 25,80±1,30kp dan 28,4±1,50. Sedangkan kerapuhan tablet matrik adalah 0,59±0,08%; 0,82±0,03% dan 0,92±0,04% berturut - turut untuk tablet matrik F4, F5 dan F6. Dari uji fisik tersebut didapatkan bahwa formula F4, F5 dan F6 memenuhi syarat fisik untuk suatu sediaan tablet.

Dari uji pelepasan diketahui bahwa hanya tablet matrik F6 yang memenuhi persyaratan pelepasan untuk sediaan lepas lambat, yaitu pada t 0,25 D (3 jam) adalah 50,03±1,56% , berada dalam rentang persyaratan 20 – 50 % dan pada t 0,50 (6 jam) pelepasannya adalah 74,24±0,91%, berada didalam rentang persyaratan 45-75%. Mekanisme pelepasan Na diklofenak dari tablet matrik F6 adalah difusi non Fickian (anomali transport)(n=0,5005) dengan kinetika pelepasan mengikuti persamaan order satu (R^2– 0,9945).

Dari hasil penelitian ini perlu dilakukan penelitian lebih lanjut yaitu uji pelepasan secara *in vivo* dari F6, sehingga dari formula tersebut dapat digunakan untuk memproduksi suatu sediaan lepas lambat dari Na diklofenak.

SUMMARY

THE DEVELOPMENT OF THE SUSTAINED RELEASE DOSAGE FORM OF DICLOFENAC SODIUM BASED ETHYLCELLULOSE - PVP K-30 MATRIX

To reduce adverse effects that happened due to the use of diclofenac sodium, the form of the sustained release dosage form from diclofenac sodium has been developed. Apart from reducing the adverse effects, the form of the sustained release dosage form of diclofenac sodium could reduce the use frequency, reduce the fluctuation of drug levels, better pattient compliance and, in general more efficient delivery of the drugs.

On the use of ethylcellulose as the sustained release matrix of diclofenac sodium by direct compression, the inhibition lasted only 2 hours. It was because ethylcellulose had a relaxation during the dissolution test. At the ethylcellulose chain–which had a relaxation–would erode quickly during the dissolution test, so the inhibiting dosage form towards the drug were small.

To reduce the quickly erosion due to the relaxation from ethylcellulose chain, combination between ethylcellulose and polyvinylpyrrolidone (PVP) K-30 was developed in this research. PVP K 30 in the dissolution media would swelling and formed a viscouse layer, so that the matrix erosion process moved slowly, and so did the release of diclofenac sodium from the matrix.

First, a formula of diclofenac sodium - ethylcellulose by comparisons of 1:2, 1:3, and 1:4 (F1, F2, and F3) was made. From the formula, granule was made with 96% ethanol solvent, sieved using 14 mesh screen, and dried in hot air oven at temperature of 50° for 2 hours. The granule was sieved using 20 mesh screen, and was patched with mesh screen 80. The patched granule in the mesh screen 80, was then added with 1% of Mg stearat and evaluated for humidity and drug content. The granules were compressed into matrix tablet with a hydraulic laboratory press by compression power of 4 tons, 30 seconds. The dose of diclofenac sodium used for each tablet was 100 mg.The physical test was conducted at matrix tablet on the hardness and friability of the tablet matrix. The release of diclofenac sodium from matrix tablet were evaluated by in vitro using a dissolution test apparatus by dissolution media pH 6.8 phosphate buffer.

From the release test of F1, F2, and F3 showed that F2 is the most appropriate one to be developed as a sustained release preparation by adding PVP K-30. Then, F2 was added with various percentages of PVP K-30 (5%, 10%, and 15% towards ethylcellulose) as F4, F5, and F6.

From F4, F5, and F6 formulas, granulation, tabletation and evaluation processes was applied here by the same method as F1, F2, and F3. The hardness of F4, F5, and F5 matrix tablets respectively were 20.46±0.79 kp; 25.89±1.23 kp; and 28.49±1.38. Meanwhile, the friability of the matrix tablets of F4, F5, and F6 respectively were 0.59±0.08%; 0.82±0.03% and 0.92±0.04%. From the physical test showed that F4, F5, and F6 formulas fulfilled the physical requirements for a tablet dosage form.

The release test showed that the only F6 matrix tablet which fulfilled the release requirements for a sustained release preparation, was at t 0.25 D (3 hours) and the release was 50.03 ± 1.56% in the range of requirements of 20-50%

ABSTRACT

THE DEVELOPMENT OF THE SUSTAINED RELEASE DOSAGE FORM OF DICLOFENAC SODIUM BASED ETHYLCELLULOSE - PVP K-30 MATRIX

The influence of adding polyvinylpirrolidone (PVP) K-30 into ethylcellulose towards releasing properties of diclofenac sodium had been examined. The result of the research was expected to be used for developing the form of the sustained release dosage form of matrix system of diclofenac sodium by using ethylcellulose and polyvinilpirrolidone K30.

The methods of this research were (1) granulation of diclofenac sodium - ethylcellulose-PVP K-30, (2) granule test, (3) compress the granule into matrix tablet, (4) matrix tablet physical test, and (5) Release test of diclofenac sodium from matrix tablet. Optimizing comparison between diclofenac sodium - ethylcellulose – which can give the best release – was applied and was then combined with PVP K-30. Formula of diclofenac sodium - ethylcellulose of 1:2, 1:3, and 1:4 was arranged and then respectively was so-called F1, F2, and F3. Granulation was conducted by using wet granulation method using 96% of ethanol as the granulating solution. The granules were evaluated for humidity and drug content. The granules were compressed into matrix tablet with a dose of diclofenac sodium of 100 mg for each tablet. The physical test was conducted at matrix tablet on the hardness and friability of the tablet. For release test of diclofenac sodium, it was conducted by in vitro through a dissolution test in the phosphate buffer (pH = 6.8).

The result of release testing of diclofenac sodium from matrix tablet of F1, F2, and F3 showed that F2 is the best optimum formula. In the F2 formula, PVP K-30 of 5%, 10%, and 15% was then added (towards ethylcellulose), and then was respectively called F4, F5, and F6. The same granulation, compression and evaluation processes as F1, F2, and F3 formulas were also applied at F4, F5, and F6. After conducting the release test, it showed that F4 and F5 cannot fulfill the release requirements for a sustained release dosage form. Meanwhile, F6 can fulfill the release requirements for a sustained release dosage form. The release mechanism of diclofenac sodium from F6 matrix tablet was non Fickian diffusion (n=0.5005) and follow a first order release pattern (R^2 =0.9945).

Keywords: *diclofenac sodium, ethylcellulose, PVP K-30, sustained release, ethylcellulose – PVP K-30 matrix*