http://www.pjbs.org

PJBS

ISSN 1028-8880

Pakistan Journal of Biological Sciences

ANSInet
Asian Network for Scientific Information
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan

Pakistan Journal of Biological Sciences 7 (5): 772-776, 2004
ISSN 1028-8880

Effect of Waxy Materials on the Release Kinetics of Ibuprofen from HPMC Based Sustained Release Matrix Tablet

Md. Belal Hossain, Mamunur Rashid and A.K.M. Motahar Hossain
Department of Pharmacy, University of Rajshahi, Rajshahi-6205, Bangladesh

Abstract: The aim of the present study was to investigate the release of ibuprofen (IB) from matrix tablets using a combination of water insoluble waxy materials with hydrophilic polymers. The waxy materials were added as additives to the hydrophilic polymer, hydroxy propyl methyl cellulose (HPMC). Bees wax (BW), cetyl alcohol (CA) and stearic acid (SA) used as waxy materials that were added in increasing amount (up to 30% of total weight of tablet) to the HPMC based sustained release (SR) matrix tablets. The results showed that the matrix tablets using all the additives released the drug by zero order mechanism. Addition of waxy materials into the matrix significantly decreased the rate of drug release due to the reduction in penetration of the dissolution fluid. From the release profiles excellent correlation was found between the concentration of waxy materials and ibuprofen release rate.

Key words: Sustained release, matrix tablet, Ibuprofen, release kinetics

INTRODUCTION

So far, it has been reported that many different types of controlled-release dosage forms have been developed to improve clinical efficacy of drug and patient compliance[1-2]. A number of methods and approaches have been used in their formulation and are well reviewed[3]. The term matrix tablet describe a tablet in which the drug is embedded in a skeleton of non-dissolving material. It needs simply direct compression of blended drugs, retardant materials and additives to form tablets. It is one of the least complicated approaches to manufacture sustained release dosage form that consists of a drug dispersed in a polymer, the polymer playing the role of a matrix[4-7]. Alternatively, retardant drug blends may granulated prior to compression. Microfine pores within the insoluble matrix effectively regulate the passage of drug from the matrix to the depot fluid. The matrix tablet, which incorporates the active ingredient in an inert material matrix, has been well known to act as an effective sustained release medicament[8].

It was found that the choice of matrix material, amount of drug incorporated in matrix, the hardness of the tablet, density variation and tablet shape could markedly affect the release rate of drug[9]. Several other workers[10-11] also reported that the rate of drug release from matrix is affected by the composition of the matrix, shape, pH of dissolution fluid, drug solubility, external agitation, amount of drug and the porosity of the matrix.

Non-steroidal anti-inflammatory drugs (NSAIDs) are usually good candidates for the development of controlled release preparations. Ibuprofen, a prominent NSAID was selected in this experiment. It possesses analgesic, anti-inflammatory and anti-pyretic activities. Chemically ibuprofen is 2-(p-isobutylphenyl) propionic acid, bearing the molecular formula $C_{13}H_{18}O_2$. Ibuprofen is indicated for symptomatic relief of rheumatoid arthritis and osteoarthritis. Its most frequent adverse effects are gastrointestinal disturbances e.g., GI ulcer and bleeding. This drug is readily absorbed orally and plasma peak levels are reached within 2 h of administration. The elimination of ibuprofen from plasma is first order with apparent half-life of 1.4 to 2.5 h.

The objective of this research was to observe the influence of different concentrations of BW, CA and SA in hydrophilic polymer matrix tablets on the kinetics, rate and the mechanism o f drug release.

MATERIALS AND METHODS

Materials: Ibuprofen (IB) (Fluka, Switzerland), Bees wax (BW) (Fluka, Switzerland), Cetyl alcohol (CA) (Fluka, Switzerland), Stearic acid (SA) (BDH, England), Hydroxy propyl methyl cellulose 50 cps (HPMC) (Fluka, Switzerland), Magnesium stearate (MS) (BDH, England). All other chemicals or reagents were of analytical grade.

Electrolab Tablet Dissolution Tester. U.S.P. (XXI) TDT-06 for dissolution, a mini drum mixer for mixing purpose, a double beam spectrophotometer (UV-1200)

Corresponding Author: A.K.M. Motahar Hossain, Assistant Professor, Department of Pharmacy, University of Rajshahi, Rajshahi-6205, Bangladesh, Tel. +88-0721-750041/Ext. 4110, Fax: +88-0721-750064 E-mail: motahar13@yahoo.com

Table 1: Amount of IB, HPMC, BW, CA and SA for various batches of matrix tablets. (Each batch contains twenty matrix tablets each weighing 200 mg)

			Amount of BW		Amount of CA		Amount of SA	
Batch No.	Amount of IB (mg)	Amount of HPMC (mg)	%	Weight (mg)	%	Weight (mg)	%	Weight (mg)
B_1	50	120	15	30	0	0	0	0
B_2	50	110	20	40	0	0	0	0
B_3	50	100	25	50	0	0	0	0
B_4	50	90	30	60	0	0	0	0
C_1	50	120	0	0	15	30	0	0
C_2	50	110	0	0	20	40	0	0
C_3	50	100	0	0	25	50	0	0
C_4	50	90	0	0	30	60	0	0
S_1	50	120	0	0	0	0	15	30
S_2	50	110	0	0	0	0	20	40
S_3	50	100	0	0	0	0	25	50
S_4	50	90	0	0	0	0	30	60

(Shimadzu, Japan) for absorbance determination and Perkin-Elmer compressor machine for tablet compression.

Preparation of matrix tablets: Twelve batches of matrix tablets were prepared for this study. In each batch 20 matrix tablets were prepared. Bees wax (BW), cetyl alcohol (CA) and stearic acid (SA) were used for matrix formulation in the batches B_1 to B_4, C_1 to C_4 and S_1 to S_4, respectively. For the preparation of HPMC based matrix tablets containing BW, ibuprofen was mixed well with HPMC in a beaker. In another beaker BW was taken and heated on a hot plate just to melt the wax. The mixer of drug and HPMC was then incorporated into the molten wax and mixed well while hot and finally cooled. Congealed mass was then passed through sieve (mesh 20) to obtain granules. The prepared granules were compressed to matrix tablets in a single punch tablet machine. Magnesium stearate was used as lubricating agent for the punch and die surface. The same procedure was followed for the preparation of matrix tablets containing CA and SA. For tablets of batches C_1 to C_4 cetyl alcohol and for batches S_1 to S_4 stearic acid were used instead of BW. The amounts of each ingredient are shown in Table 1.

Dissolution studies: The dissolution studies were carried out using two matrix tablets from each batch using an "Electrolab Dissolution Tester USP (XXI) TDT-06". One litre of phosphate buffer solution of pH 7.2 was used in each vessel (total six vessels) as dissolution medium. The temperature of dissolution medium was set at 37°C and paddle rotation was set at 100 rpm. Time was recorded as soon as the tablets were put into the dissolution vessels.

Five ml sample was withdrawn from each vessel at appropriate time intervals (5, 10, 20, 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330, 360 minutes) for the analysis of drug content. The same amount of fresh phosphate buffer was added immediately to the dissolution medium to compensate the volume. The dissolution study was carried out for 6 h.

Analysis of drug content: The extent of release of IB from each matrix tablet was measured at 223 nm wavelength using Shimadzu UV-1200 spectrophotometer. The phosphate buffer of pH 7.2 was used as blank. The absorbance data was processed by a computer and consequently the percent releases of the drug at different time were obtained.

RESULTS AND DISCUSSION

The results showed that with the increase of the waxy materials (BW, CA and SA) in the HPMC based sustained release matrix tablets the release of the drug (IB) was slowly decreased. This investigation was carried out using the waxy materials from 15-30% in the matrix tablets. The investigation displayed that the released was slowest with 30% of the waxy materials among the range

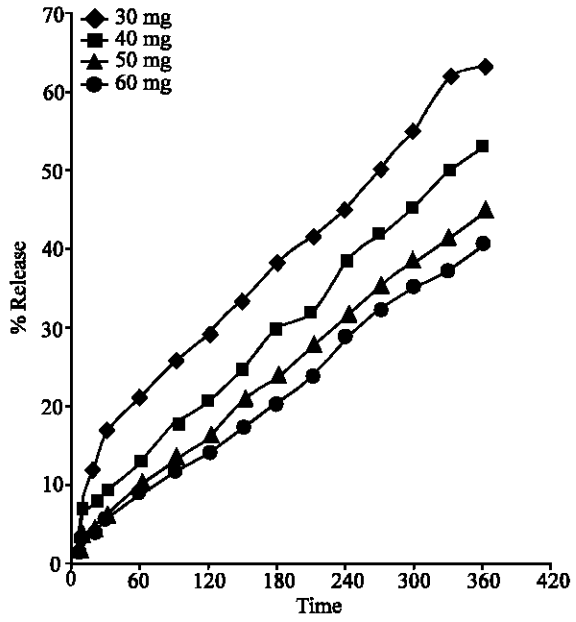

Fig. 1: Zero order plot of IB release from HPMC and BW combination matrix tablets

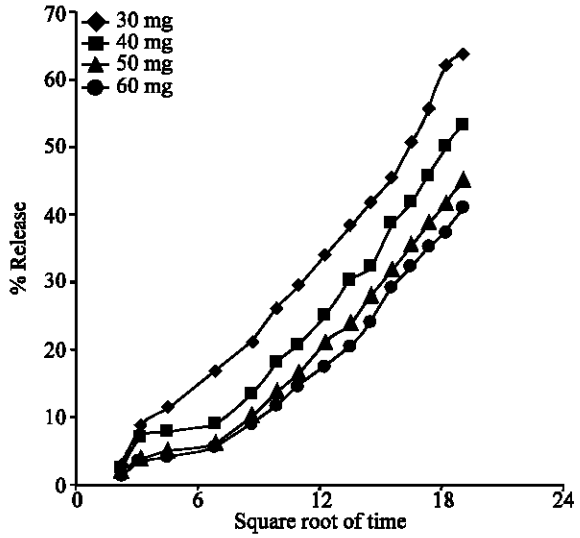

Fig. 2: "Higuchi" plot of IB release from HPMC and BW combination matrix tablets

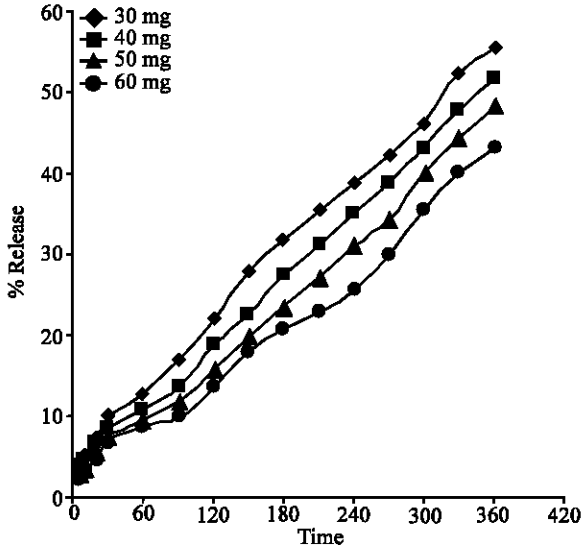

Fig. 3: Zero order plot of IB release from HPMC and CA combination matrix tablets

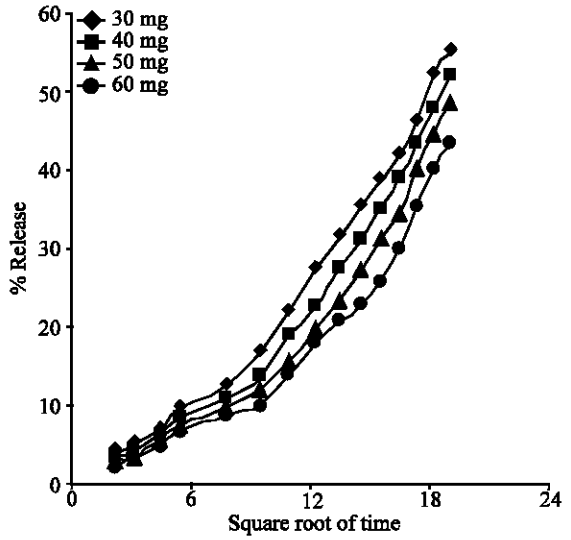

Fig. 4: "Higuchi" plot of IB release from HPMC and CA combination matrix tablets

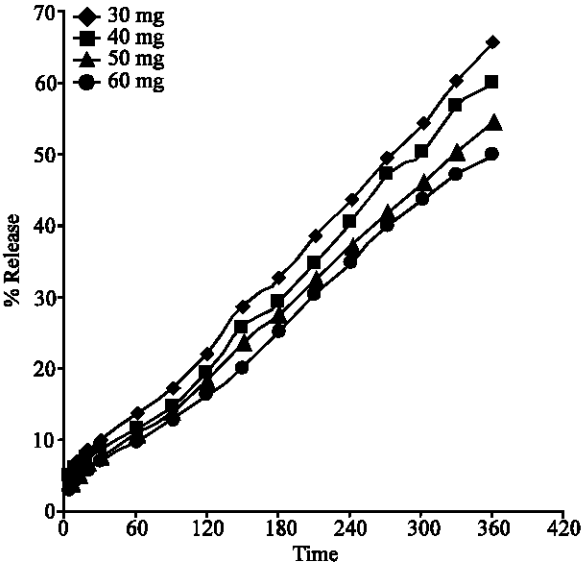

Fig. 5: Zero order plot of IB release from HPMC and SA combination matrix tablets

used in comparison with the matrix tablets using 15-30% of waxy materials. In this study, HPMC used was the hydrophilic in nature and on other hand the waxy materials used were the hydrophobic in nature. For the mixed hydrophobic/hydrophilic matrix system under investigation, drug release involves (1) penetration of the solvent into the matrix, (2) hydration and swelling of the polymer and dissolution of the active ingredients and (3) transfer of the dissolve drug and the soluble matrix components into the bulk[12].

In the present investigation, it was observed that the release of IB from matrix tablets containing BW followed zero order mechanism (Fig. 1). Higuchi plot (Fig. 2) showed slightly curved release pattern. The release of drug from the HPMC based hydrophilic matrix tablets decreased slowly with increasing the percent of BW. This may be due to the tacky nature of the hydrophobic BW that inhibits the dissolution of the drug. Ford *et al.*[13] reported that the release characteristics of drug from HPMC matrices were influenced by the diluents, drug solubility and HPMC/drug ratio. Thus the results suggested that the slowing of the drug release from the HPMC matrices was due to the wetting and the

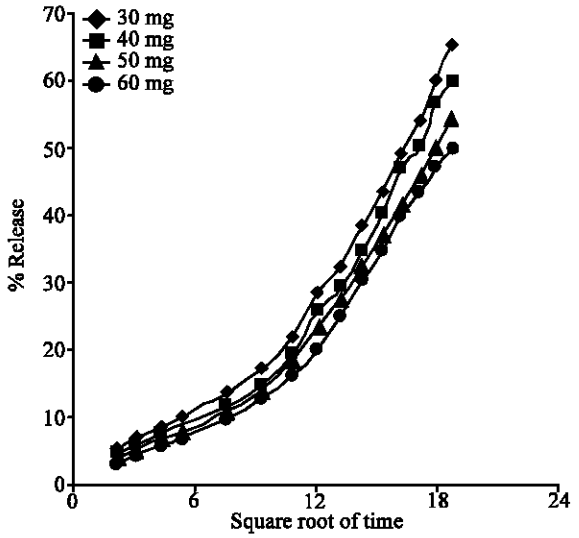

Fig. 6: "Higuchi" plot of IB release from HPMC and SA combination matrix tablets

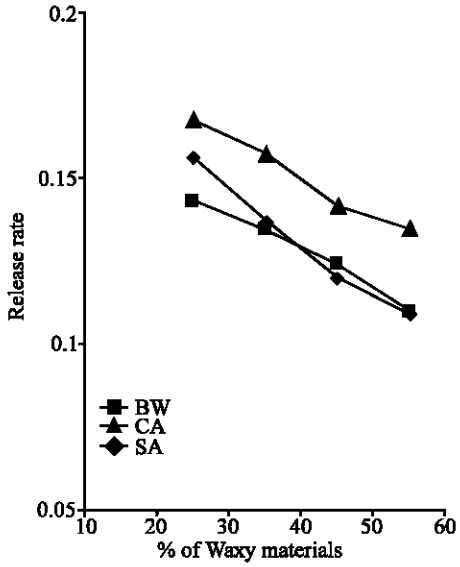

Fig. 7: Comparison of zero order release rate of IB against percent (%) of BW, CA and SA in the matrix

penetration of the dissolution fluid into the hydrophilic matrices that was prohibited by BW.

The results also showed that the release of IB from the matrix tablets containing CA and SA waxy materials showed zero order mechanism (Fig. 3 and 4). Higuchi plot (Fig. 5 and 6) for this case showed curved release pattern as well. This indicated that the release of drug from the matrices containing CA and SA followed a similar release pattern of BW. The release pattern was not influenced by changing the water insoluble waxy materials.

We have calculated the release rates of drug from all matrices contained BW, CA and SA from their respective slope values of Fig. 1, 3 and 5 and the values were plotted against the percent of the waxy materials used in this study as depicted in Fig. 7. The results revealed that the release rate was decreased with the increase of the waxy materials. Schroeder *et al.*[14] reported that the drug-wax combinations were strictly physical and the release of the drug from the waxy materials was influenced by the hardness and the composition of the core and drug particle size. Therefore, the investigation suggests that the drug release from the mixed hydrophilic and hydrophobic matrices may be influenced by the hydrophobic nature of the waxy materials and also by the hardening of the matrix and particle size of the matrix core. The result also showed that the release rate from SA containing matrix was slowest in comparison with the release rate from CA and BW containing matrix.

The purpose of the preparation of the matrix tablets using several waxy materials was to investigate the release kinetics of IB and to observe the effect of BW, CA and SA on the release profile of IB from HPMC based matrices. With the addition of hydrophobic waxy materials (BW, CA and SA) to the hydrophilic polymer (HPMC), a substantial reduction of release and release rate were observed. The release mechanism followed zero order pattern and the observed result indicates that this technology may be used to formulate SR matrix tablets with Ibuprofen and drug release could be modulated by using BW, CA and SA as release modifiers.

REFERENCES

1. Merkus FWHM., 1986. In: Rate controlled drug administration and action. Struyker-Boudier, CRC Press, Boca Raton, FL, pp: 15-47.
2. George, M., I.V. Grass and J.R. Robinson, 1989. Sustained and controlled release drug delivery systems. In: Modern Pharmaceutics (Banker G.S., Rhodes C.T. Eds.), 2nd Edn., Marcel Dekker, New York, pp: 575-609.
3. Lee, V.H.L. and J.R. Robinson, 1978. In: Sustained and Controlled Release Drug Delivery Systems (J.R. Robinson Eds.), Marcel Dekker Inc., New York, pp: 123.
4. Focher, B., A. Marzetti, V. Sarto, P.L. Baltrame and F. Carmitti, 1984. Cellulosic materials: Structure and enzymatic hydrolysis relationships. J Appl. Polym. Sci., 29: 3329-3338.
5. Droin, A., C. Chaumat, M. Rollet, J.L. Taverdet and J.M. Vernaud, 1985. Model of matter transfers between sodium salicylate-Eudragit matrix and gastric liquid. Int. J. Pharm., 27: 233-243.

6. Armand, J.Y., F. Magnard, J. Bouzon, M. Rollet, J.L. Taverdet and J.M. Vernaud, 1987. Modelling of the release of drug in gastric liquid from spheric galenics form with eudragit matrix. Int. J. Pharm., 40: 33-41.
7. Bidah, D. and J.M. Vernaud, 1990. Kinetics of *in vitro* release of sodium salicylate-eudragit matrix and gastric liquid. Int. J. Pharm., 27: 233-243.
8. Lazarus, J. and J. Copper, 1961. Absorption, testing and clinical evaluation of oral prolonged-action drugs. J. Pharm. Sci., 50: 715-732.
9. Capan, Y. 1989. Influence of technological factors on formulation of sustained release tablets. Drug Dev. Ind. Pharm.,15: 927-956.
10. Desai, S.J., 1965. Simonelli AP and Higuchi WI. Investigation of factors influencing release rate of solid drug dispersed in inert matrices. Int. J. Pharm., 54,:1459-1464.
11. Farhadieh, B., S. Borodkin and J.D. Budden-Hugen, 1971. Drug release from methyl acrylate-methyl methacrylate copolymer matrix: Kinetics of Release. J. Pharm. Sci., 60: 209-212.
12. Malamatoris, S. and D. Ganderton, 1991. Sustained release from matrix system comprising hydrophobic and hydrophilic (gel-forming) parts. Int. J. Pharm., 70: 69-75.
13. Ford, J.L., M.H. Rubinstein, J.E. Hogan, F. Mc Can and J. Edgar, 1987. Importance of drug type, tablet shape and added diluents on drug release kinetics from HPMC matrix tablets. Int. J. Pharm., 40: 223-234.
14. Schroeder, H.G., A. Dakkuri and P.P. Deluca, 1978. Sustained release from inert wax matrixes 1: Drug-wax combinations. J. Pharm. Sci., 67: 350-353.