

# Design and Evaluation of Sustained Release Matrix Tablets of Indomethacin by Employing Gelucires and Badam Gum

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## Abstract

Sustained release matrix tablets of indomethacin (IM) were developed by employing a relatively less used hydrophilic polymer badam gum and gelucires. The dissolution rate of IM is first improved by dispersing the drug in hydrophilic gelucire (50/13) and the dispersion is then embedded in the matrix of badam gum and hydrophobic gelucire (43/01). Different ratios of IM and gelucire (50/13) were employed, and the solid dispersions were prepared by melting and solvent methods. The dispersion prepared by employing solvent method resulted in much higher dissolving product than was possible with the melting method. The differential scanning calorimetry and infrared spectroscopy (IR) studies revealed that there are no interactions between IM and gelucire and the XRD studies indicated that the drug IM existed in amorphous state in gelucire dispersion. Matrix tablets were prepared by direct compression employing different proportions of badam gum and gelucire (43/01). The prepared tablets were found to be of optimum hardness, uniform weight and acceptable friability. The drug release was found to be dependent on the ratio drug: Gelucire in the solid dispersion and also on the proportion of the release retarding polymer employed – gelucire (43/01) or badam gum. The drug release data suggested that the release of the drug is the first order and is diffusion controlled

**Key words:** Badam gum, gelucires, indomethacin, matrix tablet, sustained release

## INTRODUCTION

Development of sustained release drug delivery systems provides an uniform concentration or amount of drug at absorption site, maintains plasma concentration within the therapeutic range, minimizes the side-effects and reduces the frequency of drug administration.<sup>[1]</sup> Preparation of sustained release formulation by matrix technique is a commonly employed method because of the ease of preparation, flexibility, and cost-efficiency. Compressed hydrophilic matrices are commonly used as oral drug delivery systems because of their good compatibility. Drug release from hydrophilic matrix tablets is controlled by formation of a hydrated viscous layer around the tablet, which acts as a barrier to drug release by opposing penetration of water into tablet and also movement of dissolved solutes out of the matrix tablets. The overall drug release process is influenced not only by drug solubility but also

by the physical and mechanical properties of the gel barrier that forms around the tablet. The extent of matrix swelling, erosion, and diffusion of drug determine the kinetics as well as the mechanism of drug release.<sup>[2]</sup> A number of polymers are investigated to develop *in situ* gel-forming systems. The adjustment of polymer concentration, viscosity grade and addition of different types and levels of excipients to the matrix can modify the drug diffusivity and release rate.<sup>[3,4]</sup>

Natural gums are often preferred over synthetic materials due to their nontoxicity, low cost and free availability. However,

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natural gums have certain drawbacks like uncontrolled rate of hydration, thickening, drop in viscosity on storage and microbial contamination. To overcome these difficulties – the natural hydrophilic polymers are combined with synthetic hydrophobic polymers such as ethyl cellulose, polymethyl methacrylates, glyceryl monostearate, waxes etc., to modify the drug release.<sup>[5-7]</sup>

In the present investigation, the utility of the gum exudate of plant origin *Terminalia catappa* (badam gum), as a release retarding polymer in the oral controlled drug delivery system is investigated. There are some reports<sup>[8]</sup> on the design of sustained release formulations employing badam gum. Studies are made in this investigation to design matrix tablets by combining this polymer with other release retarding agents such as gelucires.

Gelucires are a novel class of synthetic polymers derived from mixtures of mono-, di-, and triglycerides with polyethylene glycol (PEG) esters of fatty acids. Gelucires are available with a range of properties depending on their hydrophilic-lipophilic balance (1–18) and melting point (33°C–65°C) range. The gelucires containing only PEG esters (Gelucire 50/13) are generally used in preparation of fast-release formulations, while gelucires containing only glycerides or a mixture of glycerides and PEG esters (gelucire 54/02, 43/01) are used in the preparation of sustained release formulations.<sup>[9,10]</sup>

Indomethacin (IM) a poorly water soluble anti-inflammatory agent is taken as model drug. It is used in the symptomatic management of painful and inflammatory conditions such as rheumatoid arthritis and osteoarthritis. The traditional dosage forms of IM such as tablets and capsules have to be taken 3 or 4 times/day at a dose of 25 mg and it is reported<sup>[11]</sup> that 75 mg of extended release IM is clinically more effective. It has a short biological half-life of 2.5 h.<sup>[12]</sup> Administration of IM in sustained release dosage forms greatly reduces the incidence of side-effects.

Developing sustained release dosage forms for poorly soluble drugs is challenging. Because the release of the drug from the matrix system depends on the drug dissolution and subsequent release from the matrix. In this regard, it is anticipated that difficulties may be encountered to design the matrix tablets for the relatively water insoluble drugs such as IM.

A novel approach is employed in this investigation to obtain sustained release of IM wherein the very slow dissolution of IM is first overcome by dispersing the drug in gelucire (50/13) and then entrapping the fast dissolving dispersion in the polymer matrix of badam gum. The effect of adding gelucire (43/01) into the matrix formula is also studied.

## MATERIALS AND METHODS

### Materials

Indomethacin is a gift sample from Julphar Gulf Pharmaceutical Industries, UAE, gelucire (43/01) and gelucire (50/13), are obtained from Genova Life Sciences, Bangalore, India. Badam gum (grade 1) is procured from Harekrishna Herbals, Kakinada, India. All other excipients, chemicals and solvents are of analytical grade and were purchased commercially.

### Preparation of solid dispersions of indomethacin

Solid dispersions were prepared by solvent and melting methods.

#### Solvent method

Solid dispersions of IM in gelucire 50/13 (G) were prepared in two ratios (IM: G), 9: 1 and 4: 1. IM (900 mg) was dissolved in 100 ml of methylene chloride. To the clear solution of the drug, gelucire (100 mg) was added and stirred to dissolve. The solvent is removed under vacuum and the mass obtained was scrapped and dried in a desiccator over anhydrous calcium chloride overnight and was crushed, pulverized and sifted through mesh No. 100 and stored in a desiccator until further use.

#### Melting method

Dispersions were prepared in 2 ratios (IM:G) 9:1 and 4:1. Gelucire (900 mg) is first melted by heating at 60°C in a porcelain dish. The drug IM (900 mg) is now dispersed in the molten gelucire with continuous stirring for 5 min. The mixture is kept in the freezer for 6 h and then the mass obtained is crushed, pulverized and sifted through mesh No. 100 and stored in a desiccator until further use.

### Evaluation of solid preparations

#### Drug content uniformity

From each batch, four samples of 50 mg each was taken and analyzed for IM content. 50 mg of solid dispersion was weighed into a 50 ml volumetric flask. 40 ml of methanol was added and contents were thoroughly mixed to dissolve IM from the solid dispersions. The solution was made up to volume with methanol and suitably diluted with phosphate buffer of pH - 7.4 and assayed for IM content by measuring absorbance at 318 nm using phosphate buffer of pH - 7.4 as blank. The results are given in Table 1.

### Dissolution studies

The dissolution of IM in pure form and from various solid dispersions was studied using USP Type II dissolution rate test apparatus (Lab India Model DISSO) employing a paddle stirrer. In 900 ml of dissolution medium (phosphate buffer of pH - 7.4), a sample equivalent to 25 mg of IM was added and a speed of 50 rpm and a temperature of  $37^{\circ}\text{C} \pm 1^{\circ}\text{C}$  were employed in each test. A 5 ml aliquot of dissolution medium was withdrawn at different time intervals, filtered, suitably diluted and assayed spectrophotometrically at 318 nm using Labomed Model UVD 2950 spectrophotometer. The percent of IM dissolved at various time intervals was calculated and plotted against time. The results are given in Table 2 and shown in Figures 1 and 2.

### X-ray diffraction studies

X-ray powder diffraction patterns of IM and its solid dispersions were obtained by using X-ray powder diffractometer, PANalytical, Model No X Pert pro employing  $\text{Cu K}\alpha$  radiation. The diffractograms were run between  $2^{\circ}$  and  $40^{\circ}$  at  $2^{\circ}/\text{min}$  in terms of  $2\theta$  angle. The operation data were as follows: Generator tension (voltage) 40 kV; generator current 30 mA. The diffractograms of IM and various solid dispersions are shown in Figure 3.

**Table 1:** IM content of various solid dispersions prepared in gelucire (50/13)

Solid dispersion	Mean $\pm$ SD (coefficient of variation) (%)
Solvent method	
IM-G (9:1)	89.99 $\pm$ 1.03 (1.14)
IM-G (4:1)	80.24 $\pm$ 0.59 (0.73)
Melting method	
IM-G (9:1)	90.59 $\pm$ 0.23 (0.25)
IM-G (4:1)	79.96 $\pm$ 0.15 (0.18)

SD: Standard deviation, IM-G: Indomethacin-gelucire

**Table 2:** Dissolution parameters of various solid dispersions in phosphate buffer of pH 7.4

Solid dispersion	Dissolution efficiency (%) $\pm$ SD	Dissolution rate constant (K1) ( $\text{min}^{-1}$ )	$T_{50}$ (min)
IM	16.19 $\pm$ 1.28	0.012	>60.00
Solvent method			
IM-G (9:1)	46.49 $\pm$ 0.97	0.048	14.03
IM-G (4:1)	70.87 $\pm$ 1.11	0.080	4.29
Melting method			
IM-G (9:1)	30.03 $\pm$ 1.31	0.020	25.06
IM-G (4:1)	38.73 $\pm$ 1.65	0.023	18.03

SD: Standard deviation, IM-G: Indomethacin-gelucire

### Fourier transform infrared studies

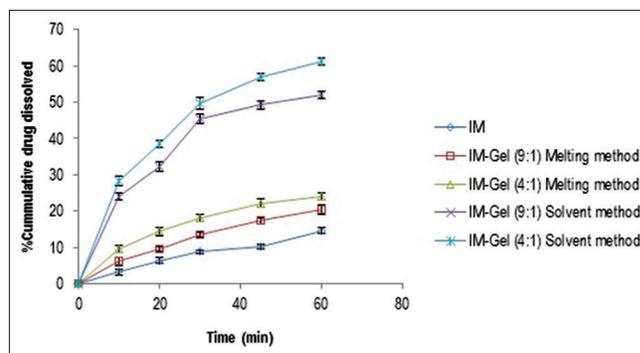
Indomethacin and the solid dispersions prepared were subjected to FTIR analysis using Fourier transform infrared spectrophotometer (Agilent Model Cary 630). Attenuated total reflectance sampling interface was used to obtain the spectra. The IR spectra are shown in Figure 4.

### Differential scanning calorimetry studies

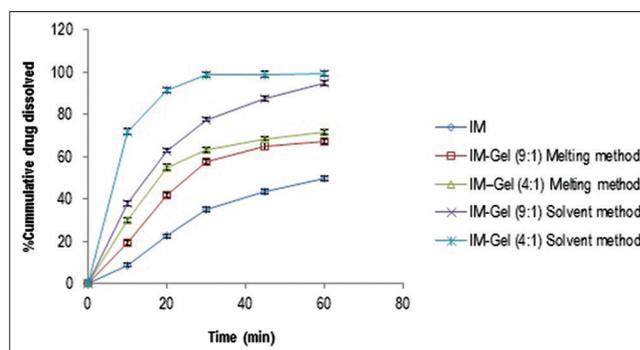
Indomethacin and the solid dispersions were subjected to differential scanning calorimetry analysis to know about the physical state of the drug in the dispersion and any interaction between the drug and gelucire. The calorimeter (TA Instruments, Bangalore Model Q 20) was operated at a scanning rate of  $10^{\circ}\text{C}/\text{min}$  and heated between  $25^{\circ}\text{C}$  to  $250^{\circ}\text{C}$ . The samples were sealed in aluminum pans and heated in a constant inert atmosphere maintained by purging nitrogen gas at a flow rate of 10 ml/min. The thermograms obtained on various products are shown in Figure 5.

### Preparation of matrix tablets employing indomethacin – gelucire solid dispersions

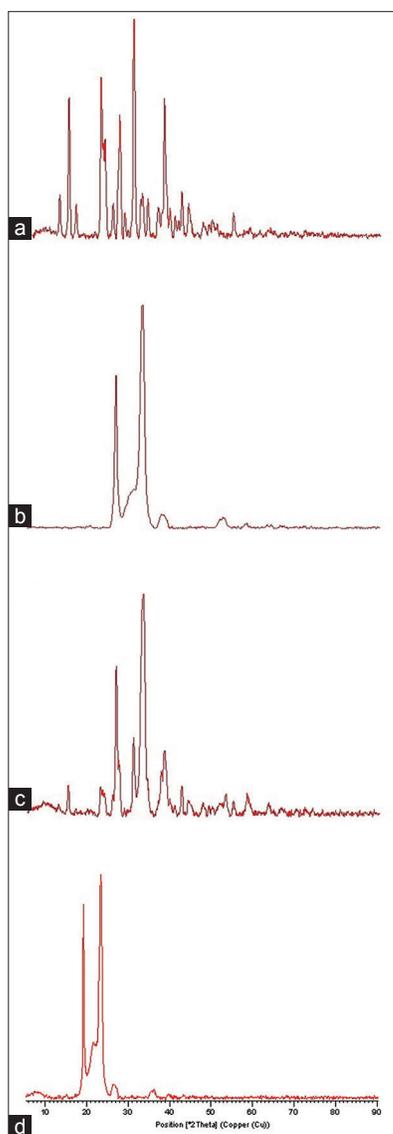
Matrix tablets of IM-G dispersions were prepared by employing the dispersions that are prepared by solvent method. This is because the dispersion prepared by solvent method gave higher dissolution than the one prepared by



**Figure 1:** Dissolution profiles of various indomethacin dispersions in 0.1 N hydrochloric acid



**Figure 2:** Dissolution profiles of various indomethacin dispersions in phosphate buffer of pH - 7.4

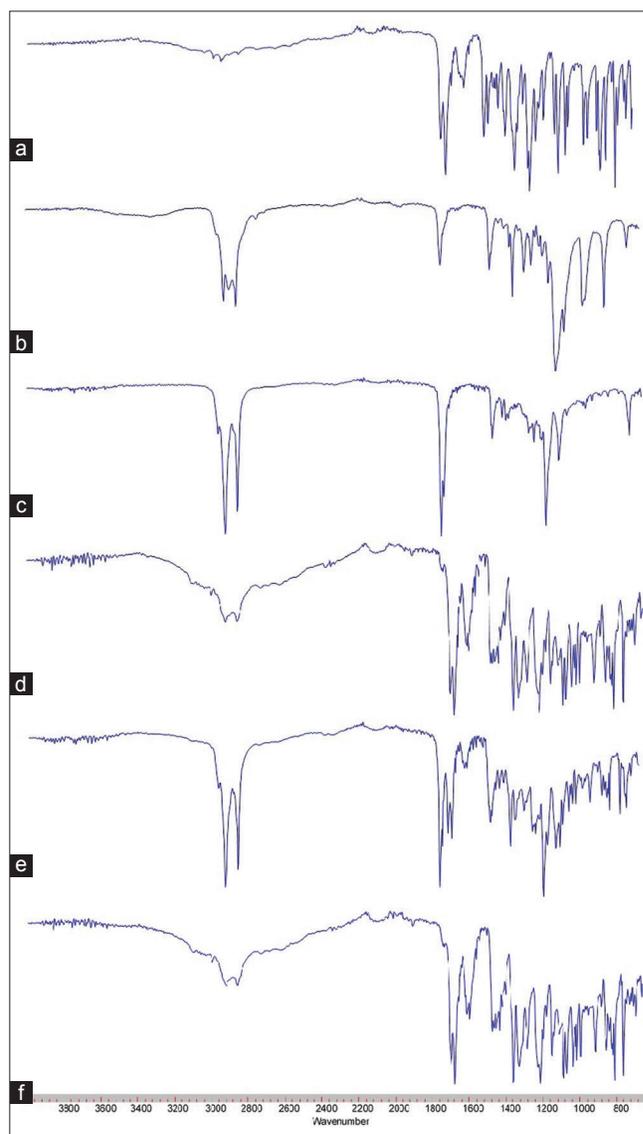


**Figure 3:** X-ray diffractograms of (a) indomethacin (IM), (b) gelucire - 50/13 (g), (c) IM: G - 4:1 solid dispersion by melting method, (d) IM: G - 4:1 solid dispersion by solvent method

melting methods (results discussed latter). Matrix tablets were prepared by employing badam gum and gelucire (43/01).

### Procedure

The formulae of various matrix tablets prepared are shown in Table 3. The dispersions and badam gum are first thoroughly blended in a mortar and rest of the ingredients are added, mixed and the mixture is subjected to direct compression employing a 16-station rotary tablet punching machine (M/s. Cadmach Machinery Co. Pvt. Ltd., India) using 9-mm round plain punches. In case of matrix tablets prepared by also employing gelucire (43/01), the solid dispersion is first mixed in molten gelucire (43/01) and then blended with rest of the ingredients and subjected to direct compression.



**Figure 4:** Infrared spectroscopy spectra of indomethacin (IM) and various products: (a) IM; (b) gelucire - 50/13; (c) gelucire - 43/01; (d) IM: Gelucire-50/13-4:1; (e) IM: Gelucire-50/13: Gelucire - 43/01 [4:1:1]; (f) formulation 6

### Evaluation of matrix tablets

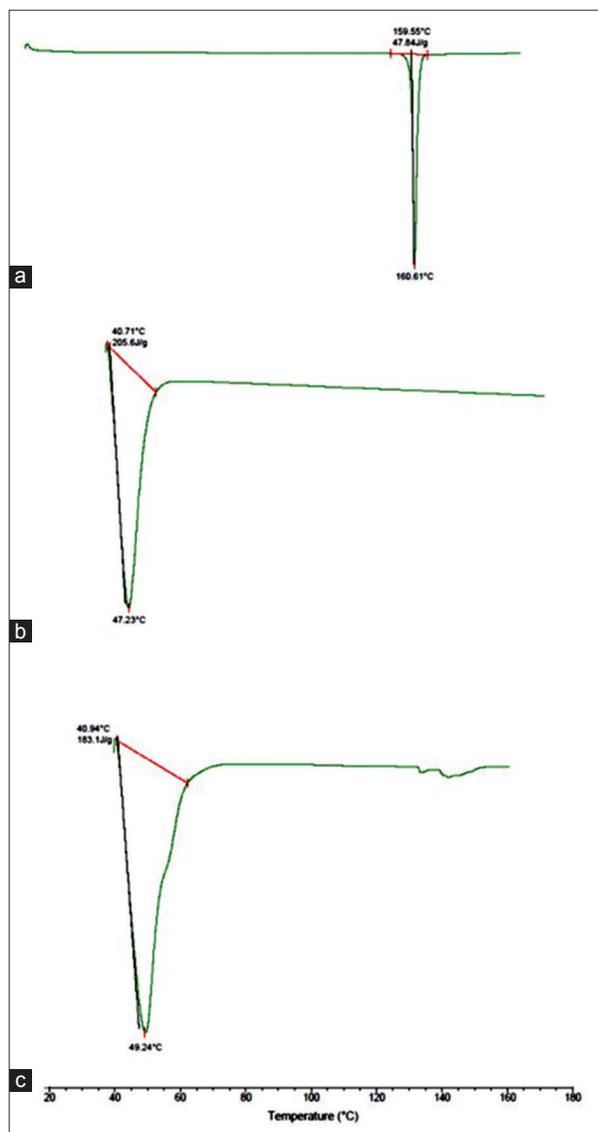
#### Drug content

Ten tablets each containing the equivalent of 75 mg of IM were collected randomly, powdered and shaken with 50 ml of methanol for 1 h. The resulting solution was diluted to 100 ml with phosphate buffer of pH - 7.4 and then filtered. The filtrate was suitably diluted and analyzed for IM content by measuring the absorbance at 318 nm.

#### Hardness

Hardness of the tablets was determined using the Monsanto hardness tester. The lower plunger was placed in contact with the tablet, and a zero reading was taken. The plunger was

then forced against a spring by tuning threaded bolts until the tablet fractured. Then the final reading was recorded. The hardness was computed by deducting the initial reading from the final reading.



**Figure 5:** Differential scanning calorimetry thermograms of (a) indomethacin (IM), (b) gelucire - 50/13, (c) IM: G - 4:1 solid dispersion by solvent method

### Weight variation

Twenty tablets were collected at random and were weighed collectively and individually. From the collective weight, average weight was calculated. The percent weight variation was calculated using formula:

$$\text{Percent weight variation} = \left( \frac{\text{Average weight} - \text{Individual weight}}{\text{Average weight}} \right) \times 100.$$

### Friability

The Roche friability test apparatus was used to determine the friability of the tablets. 20 tablets were selected, de-dusted and weighed. Then these were placed in a drum and rotated for 100 times in 4 min. The tablets were de-dusted to remove any loose dust and were re-weighed. The percentage friability was calculated by the formula.

$$\text{Percent friability} = \left( \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \right) \times 100.$$

The details of drug content, hardness, friability and weight variation are given in Table 4.

### Drug release studies

The drug release study from the prepared matrix tablets was performed by employing USP Dissolution Rate Test Apparatus Type 1 employing a basket stirrer. The drug release study is performed in 0.1 N hydrochloric acid for first 2 h and in phosphate buffer of pH 7.4 for the remaining 10 h. Samples of the medium are withdrawn at regular intervals and replaced by fresh medium, and the absorbance of the filtered samples was measured at 318 nm. The results of the drug release study are given in Table 5 and shown in Figures 6 and 7.

## RESULTS AND DISCUSSION

The initial studies performed on the dissolution of pure drug IM in 0.1 N hydrochloric acid and in phosphate buffer of pH 7.4 revealed that only about 14% and 49% respectively was dissolved in 1 h. The higher dissolution seen in phosphate buffer could be because of higher solubility of the drug in

**Table 3:** Composition of matrix tablets prepared by employing IM-G dispersion – IM-G (4:1)

Ingredient (in mg)	F1	F2	F3	F4	F5	F6
Dispersion (equivalent to 75 mg of IM)	93.75	93.75	93.75	93.75	93.75	93.75
Badam gum	25	50	75	25	25	25
Gelucire (43/01)	-	-	-	20	30	40
MCC*	71.25	46.25	21.25	51.25	41.25	31.25
Talc	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5

\*Microcrystalline cellulose – avicel. IM-G: Indomethacin-gelucire, FMC type pH - 105

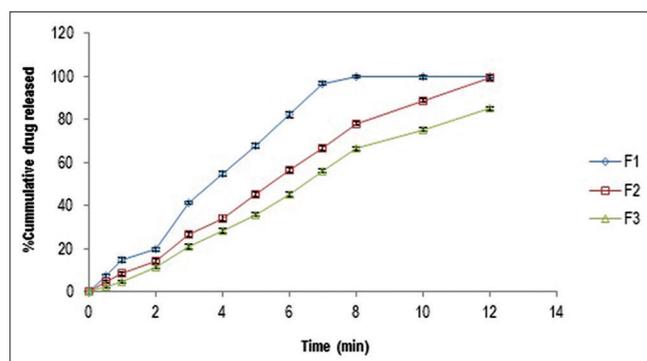
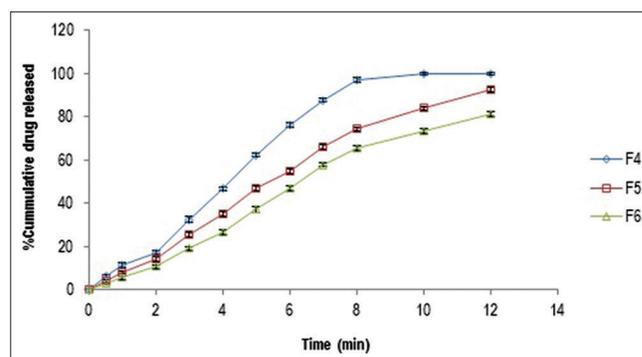
**Table 4:** Drug content, hardness, weight variation and friability of different formulations

Formulation	Drug content <sup>a</sup> (%)	Hardness <sup>b</sup> (kg/cm <sup>2</sup> )	Weight <sup>c</sup> (mg)	Friability <sup>d</sup> (%)
F1	99.12±1.09	6.11±0.25	201±0.87	0.31±0.04
F2	98.89±1.12	5.99±0.33	200±1.01	0.21±0.02
F3	99.05±0.96	5.87±0.65	199±1.15	0.18±0.01
F4	99.27±0.87	4.99±0.13	200±1.12	0.76±0.11
F5	99.57±0.99	5.21±0.43	201±0.45	0.81±0.17
F6	99.26±1.03	5.05±0.38	200±0.95	0.87±0.11

<sup>a</sup>Mean±(n=10), <sup>b</sup>n=5, <sup>c</sup>Mean±(n=20), <sup>d</sup>n=20

**Table 5:** Correlation coefficient ( $r^2$ ) values in various kinetic models and first order rate constant of various matrix tablet formulations

Formulation	Correlation coefficient ( $r^2$ )				First order constant $K_1$ (h <sup>-1</sup> )	Peppas $n$ value
	Zero order	First order	Higuchi	Peppas		
F1	0.869	0.990	0.966	0.942	0.322	0.569
F2	0.880	0.989	0.927	0.988	0.166	0.692
F3	0.927	0.988	0.956	0.998	0.131	0.748
F4	0.812	0.971	0.961	0.996	0.292	0.587
F5	0.922	0.981	0.969	0.950	0.175	0.645
F6	0.952	0.980	0.950	0.991	0.124	0.765

**Figure 6:** Indomethacin release from various matrix tablets (F1–F3)**Figure 7:** Indomethacin release from various matrix tablets (F4–F6)

alkaline medium. However, a low dissolution in the acidic medium is a disadvantage and the release may be further hindered from a sustained release matrix tablet – particularly because the administered dosage form will remain for about 2 h in the gastric fluids. For a drug to be released from a matrix tablet, its dissolution in the dissolution fluids in the matrix is a prerequisite. Thus, IM powder as such is unsuitable for preparing controlled release matrix tablets. Hence in the present work, a physically modified form of IM is prepared by solid dispersion of the drug in a water soluble carrier gelucire (50/13) to result in a more rapidly dissolving IM with the objective of verifying the feasibility of employing these dispersed forms of IM in a matrix tablet for achieving a faster, but controlled release. A study on incorporating amorphous forms of nifedipine in microcapsules for obtaining controlled release is reported by Chowdary and Ramesh.<sup>[13]</sup>

The solid dispersions of IM in gelucire are prepared by melting and solvent method. All the solid dispersions prepared were found to be fine and free flowing powders. The percent drug contents of various solid dispersions are given in Table 1. There was no significant loss of drug during the preparation of solid dispersions and the proportion of drug and carrier remained the same as that initially taken. Low standard deviation (SD) and coefficient of variation (CV) values in the percent drug content ensured uniformity of drug content in each batch.

The usual method of evaluation of *in vitro* dissolution testing is the comparison of the time taken for given proportions of active drug to be released into solution and values such as  $T_{20}$ ,  $T_{50}$  and  $T_{90}$  are often used. Another parameter suitable for the evaluation of *in vitro* dissolution

has been suggested by Khan,<sup>[14]</sup> who introduced the idea of dissolution efficiency (D.E.). D.E is defined as the area under dissolution curve up to a certain time 't' expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time.

$$\text{Dissolution efficiency (D.E.)} = \frac{\int_0^t y dt}{Y_{100} t} \times 100.$$

The D.E. can have a range of values depending on the time intervals chosen. In any case, constant time intervals should be chosen for comparison. For example, the index D.E.<sub>30</sub> related to the dissolution of the drug from a formulation after 30 min could only be compared with D.E.<sub>30</sub> of other formulations. Summation of the drug dissolution data into a single figure D.E., enables ready comparison to be made between a large numbers of formulations. The dissolution of IM in pure form and from various solid dispersions followed first-order kinetics. The dissolution plots are shown in Figures 1 and 2 and data is given in Table 2.

The dissolution of IM from various solid dispersions is found to be higher compared to that of the pure drug. This higher dissolution of IM from gelucire dispersions could be because the presence of drug in more amorphous form (as discussed below in the results of XRD analysis) and also because of the higher wettability of the drug in the dispersions. One interesting finding of our studies is that a higher dissolution was seen in products prepared by solvent method than by the melting method. This is probably because the drug is more uniformly dispersed in the polymer (gelucire) solution preventing their aggregation back again and also resulting in much smaller particle size after the solvent is removed. This resulted in a more homogeneous distribution of the drug in the polymer, whereas such an opportunity to uniformly disperse in the polymer is not available in the melting method. This probably resulted in lower dissolution for the solid dispersion prepared by melting method. Also in solvent method to obtain an almost complete dissolution in 30 min [Figure 2] – it required a lesser amount of gelucire (IM: G - 4:1) in the dispersion – whereas to obtain a product of comparable high dissolution a larger amount of gelucire (at a ratio of IM: G - 1:4) had to be employed (results not being given) in melting method. Employing such high proportion of gelucire resulted in a dispersion which is very tacky and unhandable and certainly not suitable for further processing such as compression.

The various dissolution parameters are given in Table 2. It was observed that the D.E. values of products (IM-G - 9:1 and 4:1) - 46.49% and 70.87% and dissolution rate constants - 0.048 min<sup>-1</sup> and 0.080 min<sup>-1</sup> of the products prepared by solvent method are higher than that obtained with melting method, which showed a D.E. of 30.03% and

38.73%, and dissolution rate constant of 0.020 min<sup>-1</sup> and 0.023 min<sup>-1</sup>.

### X-ray diffraction

The X-ray diffractograms of gelucire (50/13), pure drug IM and the dispersions are shown in Figure 3. It can be seen that the pure drug, which is highly crystalline as evident from the sharp diffraction peaks is converted into an amorphous form in the solid dispersions, as the crystalline peaks have disappeared. It can also be noticed that the extent of reduction in crystallinity is more with the dispersion prepared by the solvent method Figure 3d than by the melting method Figure 3c. It may be concluded that solvent method is better than the melting method in preparing more dissolving dispersion of IM in gelucires. So the increased dissolution of the drug from the solid dispersions is probably because of the crystalline drug IM being converted into an amorphous form and also because of the increased wetting action of gelucire on the drug.

## FOURIER TRANSFORM INFRARED STUDIES

Any possible interaction between IM and the polymers – gelucires and badam gum – was verified by comparing the IR spectra of pure IM with that of dispersions and the matrix tablet formulation. The IR spectra are shown in Figure 4. Pure IM (a) exhibited characteristic peaks at 1715 cm<sup>-1</sup> (C=O stretching), 1600 cm<sup>-1</sup> (aromatic C=C stretching), 1450 cm<sup>-1</sup> (O – CH<sub>3</sub> deformation), 1230 cm<sup>-1</sup> (C-O stretch plus O-H deformation), 1086 cm<sup>-1</sup> (symmetric aromatic O-H stretching). The solid dispersion (d) in gelucire (50/13) and the tablet formulation F7 (e) – also exhibited the characteristic peaks of IM indicating retention of chemical identity of IM. Hence, there was no interaction between the drug and excipients used in the study.

### Differential scanning calorimetry

The thermograms of IM and the dispersions are shown in Figure 5. The endotherm of pure drug IM showed a sharp peak at 161°C which is due to its melting point. Gelucire (50/13) showed its endothermic peak around 47°C. Whereas the sharp endothermic peak expected of IM in the gelucire dispersion disappeared almost completely. This could be due to the presence of the drug in soluble amorphous state in the polymer and complete loss of crystallinity. This finding is in agreement with Agnivesh *et al.*<sup>[15]</sup> who reported that disappearance of the characteristic peaks of the valsartan dispersed in Gelucire 50/13 is due to melting of the drug in the matrix. This loss of crystallinity and presence in soluble state resulted in faster dissolution of IM from the gelucire solid dispersions.

## Characterization of matrix tablets

The tablet formulations of all the prepared batches contained IM within  $100 \pm 5\%$  of expected content. The hardness of various prepared tablets is in the range of 4.99–6.11 and the friability is found to be  $<1\%$ . The weight variation of all tablets is found to be low. The details composition of tablet formulations are shown in Table 3 and the various physical characteristics are given in Table 4.

## Drug release

The release [Figures 6 and 7] of IM from all the matrix tablets is found to be slow and sustained. However as shown in Figure 6, there is complete release within 6–8 h itself from formulation F1. But as the amount of badam gum increased there is more retarding effect and in formulations F2 and F3 – the release could be extended upto 12 h and in fact in F3 – the retarding effect is so much that only 85% of drug was released at the end of 12 h. So to further modify the release such that it is slow and spread over 12 h – formulation F1 is altered by incorporating gelucire (43/01) which is waxy and lipophilic in nature. Keeping the proportion of gum same and increasing the proportion of gelucire (43/01) resulted in slower release (F5 and F6). While F1 released all the drug by the end of 7 h – inclusion of gelucire (43/01) prolonged the release upto 12 h. So by suitable variations in the amount of badam gum and gelucire (43/01) – the release can be modulated suitably. Of all the formulations - F5 is found to be giving a release which is complete and spread uniformly for 12 h.

To know the drug release mechanism – the data are analyzed as per zero order, first order, Higuchi<sup>[16]</sup> and Korsmeyer<sup>[17]</sup> models. The model that best fits the release data was evaluated by correlation coefficient ( $r^2$ ). The  $r^2$ - values in various models is given in Table 5. The plots of amount released versus square root of time were linear and the high  $r^2$  values suggested the drug release is by diffusion. The correlation coefficient values were higher for first order model than zero order models indicating the drug release from the matrix tablets was according to first order kinetics. According to the  $n$  values (between 0.569 and 0.765), obtained in the Peppas plot, one may conclude that the drug release follows non-Fickian anomalous diffusion. Accordingly the drug release from these matrix tablets involves penetration by dissolution fluid, dissolution of the drug in dissolution fluid and diffusion of the dissolved drug.

## CONCLUSIONS

Solid dispersion of IM in gelucire (50/13) by solvent method resulted in fast dissolving IM. Conversion of the solid dispersion into matrix tablets by direct compression employing badam gum and gelucire (43/01) produced

sustained and complete release of IM spread over a period of 12 h. The release profiles could be altered with changes in the proportion of badam gum or gelucire (43/01) in the matrix tablets. The findings of the present study suggest that employing a combination of hydrophilic and hydrophobic gelucires is a promising approach to design sustained release products of poorly soluble drugs such as IM.

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