Original Article

Investigation on *in-vitro* Dissolution and Tableting Properties Enhancement of Etodolac using Stearoyl polyoxyl-32-glycerides as Novel Solid Melt Carrier

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ABSTRACT

Objectives: The objective of present study was to improve dissolution rate with tableting properties of BCS class II drug Etodolac, by melt granulation and sublimation techniques. **Materials and Methods:** The granules of etodolac were formulated using Gelucire 50/13. The surface adsorbent Aerosil 200 was utilized. Both melt granulation and surface adsorption method in conjunction with sublimating agent were used to formulate tablets of Etodolac. Etodolac: Gelucire 50/13: Aerosil200 was used in different ratio for melt granulation technique to improve dissolution and tableting properties. **Results:** Solubility study of melt granules were carried out in different ratio. 1:2:1 ratio showed 25 fold increases in solubility of Etodolac. This 1:2:1 (A4) ratio was selected to designate the tablets along with super disintegrant and sublimating agents. Precompression and post-compression parameters results were satisfactory for etodolac tablets. XRD and DSC study showed that Etodolac crystallinity was completely disappeared in A4 melt granules. *In vitro* drug release of formulation F4 and F8 containing crosscarmallose sodium and menthol were found to be 94.64% and 98.14% drug release at the end of 24 and 20 min respectively. The dissolution statistics like MDT, %DE and DP10 for optimized formulation F8 exhibited 8.90 min, 28.25% and 55.45% respectively. **Conclusion:** The melt granulation technique is useful to improve dissolution of Etodolac ideally, along with superior tableting properties.

Key words: Etodolac, Gelucire50/13, Melt granulation, Sublimating agent, Surface adsorption, Dissolution improvement.

INTRODUCTION

The GIT region imparts sufficient fluid in the direction of making the disintegration for solid formulation furthermore dissolution. Basically massive surface vicinity of gastric mucosa positively affects the absorption of the drug. Since the oral path has sustained the utmost attractive rout for transport of drug even though the advancements made within the latest drug transport systems. Banker and Anderson confirmed that as a minimum 90% of the entire tablets preferred to supply systemic result are given by oral route. The efficiency of oral product rests on its absorption in the GIT.[1] The rate and extent of a drug rely on its solubility moreover dissolution rate. Dissolution is the rate-determining step in the onset of therapeutic activity. Consequently poorly water soluble tablets are specified via a little bioavailability as a result of a smaller amount of absorption and this is a main focus of pharmaceutical industries.[2] Nowadays, the utmost challenge in pharmaceutics is to develope oral dosage forms of Biopharmaceutical Classification System (BCS) class II or IV drugs. The abundant formulation techniques has been reported in the most recent decades to enhance the solubility moreover dissolution rate of poorly water soluble drug.[3] The methods are inclusion complexes,[4] salt formation,[5] microemulsion,[6] nanoprecipitation,[7] self-emulsifying system,[8]

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liquisolid compacts, nanotechnology[9] and crystal engineering.[10]

In the previous decade research of solid dispersion has been revealed by generous researchers. Solid dispersions designed for poorly water soluble molecules have more amplification on dissolution rate and since increase relative bioavailability.[3] Etodolac is a non-steroidal anti-inflammatory drug and used in rheumatoid arthritis. The solid dispersion technique is ordinary technique to boost the dissolution rate which can be used to increase the bioavailability of etodolac.[11]

In recent times, many researchers accounted solid dispersions by using Gelucire as amphiphilic additive.[12] It is long chain fatty acid esters of polyethylene glycol along with glycerides (mono-, di- and/or tri-esters). Gelucire is named based on its HLB value and melting point.[13] Gelucire50/13 is a hydrophilic carrier having melting point 50°C and band HLB value of 13, can usually utilized like a carrier into solid dispersion by fusion method.[14]

Even though Gelucire50/13 containing solid dispersions extensively boost the dissolution rate of poorly water soluble drugs, except these are with various boundaries as poor flow with sticking toward punches. Development of tablet dosage form is principally problematical as a result of poor flow as well as sticking. In turn to knock this problem, an inert amphiphilic carrier having excellent flow along with compressibility can be used for adsorption of the dispersion on surface.[15]

To beat this problem an inert carrier by means of excellent flow may well used for adsorption of molten carrier.[16] The inert material Aerosil 200 was used which have specific surface area 200 m^2/g. Aerosil show a little particle size in the colloidal range.[17] The silica particles help to form matrix. Further drug is molecularly dispersed in this formed matrix.[18]

Hence the purpose of present research study is improvement of solubility moreover dissolution of Etodolac by way of melt dispersion granulation using Gelucire50/13. Further Aerosil200 is used as adsorbent, to boost the flow property and compressibility of prepared melt granules. Further immediate release Etodolac tablet is formulated by using super disintegrant and sublimating agents to achieve dissolution efficiency and disintegration.

MATERIALS AND METHODS

Materials

Etodolac was kindly gifted by Ipca laboratories, Mumbai. Gelucire 50/13 provided by Gattefosse India Pvt. Ltd., Mumbai. Aerosil200 and microcrystalline cellulose were purchased from Loba Chem, Mumbai. Cross carmellose sodium as well Sodium starch glycolate were procured from Maxwell Life Sciences, Mumbai. Camphor and menthol was obtained from SDFCL, Mumbai. Other reagents, chemicals and reagents were analytical grade and purchased locally.

Methods

Formulation of melts dispersion granules of etodolac

The etodolac loaded melt dispersion granules were formulated using hot-melt granulation.[19] Briefly, weighed quantity of Gelucire50/13 was liquefied at 80°C to form lipid melt and specified quantity of Etodolac was added to this molten mass with continuous stirring on water bath. The Aerosil 200 was incorporated in drug loaded molten mass with continued mixing in next subsequent step to form melt dispersion granules of etodolac. Dispersion granules then passed through mesh No. 18. The various batches of granules were prepared by varying drug: lipid ratios as specified in Table 1.

Evaluation of etodolac melts dispersion granules

The formulated melt dispersion granules of etodolac were evaluated with respect to saturation solubility, differential scanning calorimetry, X-Ray diffraction study and micromeritics properties.

Saturation solubility study of etodolac, dispersion granules and physical mixture

The saturation solubility of etodolac, drug: excipients physical mixture and formulated melt dispersion granules were estimated in HCl buffer (pH 1.2). An excess amount of drug, physical mixture and melt dispersion granules were added in 20 ml of fresh HCl buffer separately and subjected to rotary shaker bath at room temperature for 24 hr. After 24 hr the solutions were filtered, suitably diluted and analyzed spectrophotometrically at 279 nm.

Table 1: Melt Dispersion granules containing varying ratios of Etodolac, Gelucire 50/13 and Aerosil 200.

Batch no.	Etodolac	Gelucire 50/13	Aerosil 200
A0	1	---	---
A1	1	0.5	0.25
A2	1	1	0.50
A3	1	1.5	0.75
A4	1	2	1
A5	1	2.5	1.25
A6	1	3	1.50

Drug and excipients compatibility study

The compatibility of drug and excipients was analyzed using FT-IR spectroscopy (Bruker Alpha-T, Germany). The FTIR spectrum of etodolac, Gelucire50/13 and Aerosil 200 were recorded separately using Fourier Transform Infrared Spectrometer in wavelength range 400-4000 cm^{-1}.[20]

Differential scanning calorimetry (DSC)

The DSC thermograms of etodolac, Gelucire50/13 and melt dispersion A4 were recorded separately using DSC-60 (Shimadzu, Japan) in order to investigate the effect of formulation process on the physical state of the components. Accurately weighed test samples were placed in sealed aluminum pans and heated from 30°C to 300°C at a heating rate of 5°C/m with nitrogen purging (20 ml/m) and thermal behavior was assessed.

Powder X Ray Diffraction Study

The X-ray diffraction patterns were traced using XRD analyzer (Bruker D8, Germany). Briefly, 500 mg of samples were placed on the sample holder and the sample holder was placed on the rotating sample stage. The sample was placed in the horizontal position and the X-Ray tube and the detector were moved over the sample simultaneously over the two theta angular ranges from 10° to 60° with a continuous scan rate of 4° per minute. The obtained signal pattern is represented in Figure 4.

Assessment of micromeritics properties

The assessment of tableting characteristics is necessary prior to the compression of tablet. The flow properties like angle of repose, tapped density, bulk density, Carr's compressibility index and Hausner's ratio were determined. The study performed in triplicate and average of three determinations was taken.

Preparation of Etodolac tablet

The dispersion granule formulation A4 was selected for compression of tablet.[21] Accurately weighed quantity of etodolac melt dispersion granules and excipients were mixed and compressed using 12 mm flat faces punches on 16-station rotary tablet punching machine (CADMACH, India). The CCS/SSG/camphor/menthol, talc, microcrystalline cellulose and magnesium stearate were used as excipients. After compression menthol /camphor containing tablets were placed within hot air oven on 40°C till to achieve the constant weight for activation of channels/pores in tablet. The composition of different formulations is highlighted in Table 2.

Evaluation of Etodolac tablets

The compressed etodolac tablets were evaluated with respect to thickness, weight variations, hardness, friability, disintegration time and *in-vitro* drug release. Thickness for the tablet was measured using Digital screw gauge micrometer (Yuri, Japan). The Monsanto hardness tester was used to measure tablet hardness. Friability of tablets was assessed using Roche Friabilator and disintegration time of tablets was estimated using USP disintegration test apparatus (Electrolab, India). The average of three determinations was taken and statically analysed.

Determination of content uniformity

The drug content uniformity of melt dispersion granules based tablet was assessed. The 10 tablets were weighed and crushed in glass mortar. The powder equivalent to 100 mg of etodolac was transferred to a 100 ml volumetric flask in 30 ml methanol and sonicated for 10 min. Then volume made up to 100 ml with HCl

Table 2: Formulation of Melt Dispersion Granulated Etodolac Tablets (Weights are in mg).

Ingredients	Formulation codes								
	F0	F1	F2	F3	F4	F5	F6	F7	F8
Etodolac	200	200	200	200	200	200	200	200	200
Gelucire 50/13	400	400	400	400	400	400	400	400	400
Aerosil 200	100	100	100	100	100	100	100	100	100
Sodium starch glycolate	---	36	54	---	---	---	---	---	---
Cross carmellose sodium	---	---	---	36	54	---	---	---	---
Menthol	---	---	---	---	---	45	63	---	---
Camphor	---	---	---	---	---	---	---	45	63
Micro crystalline cellulose	182	146	128	146	128	137	119	137	119
Magnesium stearate	9	9	9	9	9	9	9	9	9
Talc	9	9	9	9	9	9	9	9	9

buffer pH 1.2, same procedure was followed for the placebo tablets and used as blank. The solution subjected for filtration and samples were analyzed UV spectrophotometrically for etodolac content.[22]

In-vitro dissolution study

The USP type II dissolution apparatus was used to assess the *in-vitro* drug release. The HCl buffer pH 1.2 was used as dissolution medium. The volume and temperature of dissolution medium were 900 ml and 37 ±0.1°C. The paddles were rotated at 50 rpm. The 5 mL of aliquot was withdrawn at predetermined time intervals and analyzed for drug dissolved using spectrophotometry.[23] Based on dissolution study data the dissolution efficiency (% DE), mean dissolution time (MDT) and DP10 were calculated. The dissolution efficiency (DE) for dosage form means the area under the dissolution curve up to the time, t, expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time. MDT is considered to rate the extent of dissolution enhancement of etodolac by using the dissolution data. DP 10 is % of drug dissolved at 10 m which was calculated from graph of dissolution profile.[22] The average of three determinations was taken and statically analysed.

RESULTS AND DISCUSSION

Preparation of Melt Dispersion Granules of Etodolac

The dispersion of etodolac and Gelucire 50/13 adhered to the beaker once it dried. This led to a lesser yield of the product following poor flowability. When molten mixture of Etodolac and Gelucire 50/13 was added to the Aerosil 200 for adsorption then, it yield was increased along with increased flowability.

Saturated Solubility study for etodolac, dispersion granules and physical mixture

Solubility study of melt dispersion granules and A4PM formulation revealed increase in solubility of the drug up to 25 fold. Solubility for Etodolac was found 0.124 mg/ml (Figure 1). Gelucire50/13 improves solubility by forming hydrogen bond with drug leading to formation of stable solid amorphous drug in dispersion and surface active power increases wettability of drug. The solubility of Etodolac increases with increased ratio of Gelucire 50/13 up to 1: 2 (Etodolac: Gelucire 50/13), further increases in the Gelucire50/13 proportion showed nearly resembling solubility. Surface active nature of Gelucire 50/13 is responsible for the solubility enhancement.

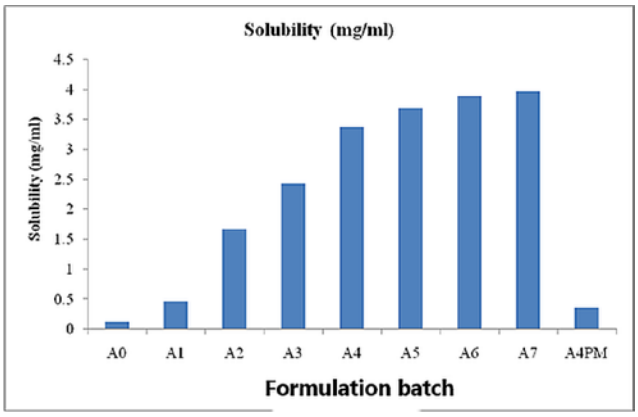

Figure 1: Saturated solubility Study of Etodolac melt dispersion granules.

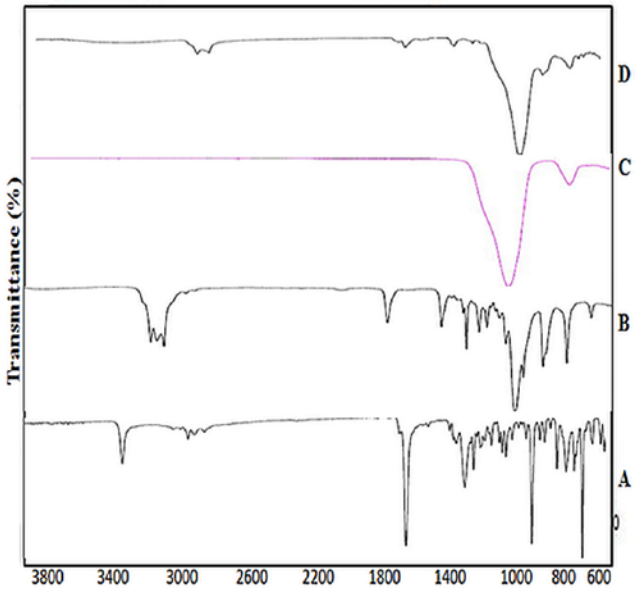

Figure 2: FT-IR Spectra of A- Etodolac, B-Gelucire 50/13, C-Aerosil 200 and D-Melt granules of A4.

Drug and excipients compatibility Study

FTIR spectrum of etodolac revealed C-O stretching at 1029 cm^{-1}. The peak at 1740 cm^{-1} revealed that it is C=O stretching vibration for the COOH group. The less intense peak at 3530cm^{-1} represented N-H stretching. The free O-H stretching vibration peak was observed at 3720 cm^{-1}. Spectra of melt granules (A4) expressed every peak of Gelucire 50/13 as well as without of affecting the positions (Figure 2). This confirms physical compatibility between drug Etodolac and binder Gelucire 50/13.

Flow properties of granules

The values of bulk density, tapped density, angle of repose, Carr's index and Hausner's ratio for melt dispersion granule A4 was expressed that the flowability

along with compressibility present in the range of theoretical values and can be processed into tablet dosage form.[12] The waxy nature of Etodolac: Gelucire 50/13 granules were made flowable by adding the Aerosil 200 to the half quantity of Gelucire50/13 in each batch of granules. The adsorption is due to the high specific surface area of the Aerosil 200.

Differential scanning calorimetry

In DSC thermogram for etodolac, a sharp endotherm at 149.11°C, revealed melting point of drug. Latent heat of fusion (ΔHfus) was 59.8J/g (Figure 3A). This endotherm signifies crystalline form of drug. The DSC thermogram of Gelucire 50/13 (Figure 3B) showed sharp endothermic peak at 49.91°C (Tfus) corresponding to its melting temperature and having latent heat of fusion (ΔHfus) 34.9J/g. The DSC thermogram of melt dispersion granules of A4 (Figure 3C) confirmed that the disappearance of etodolac characteristic endothermic peak and showed endothermic peak at 54.15°C which

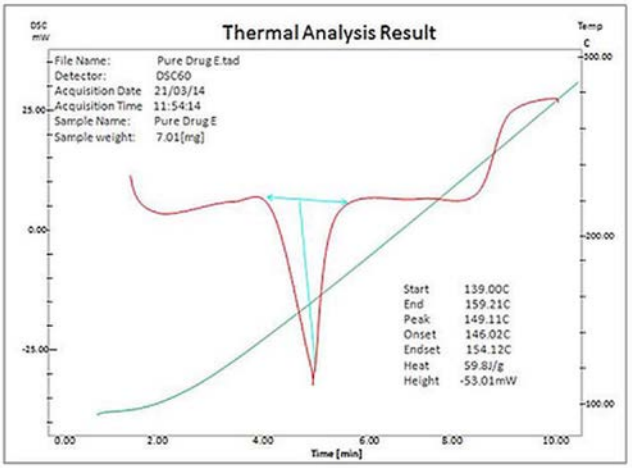

Figure 3A: DSC spectra of pure Etodolac.

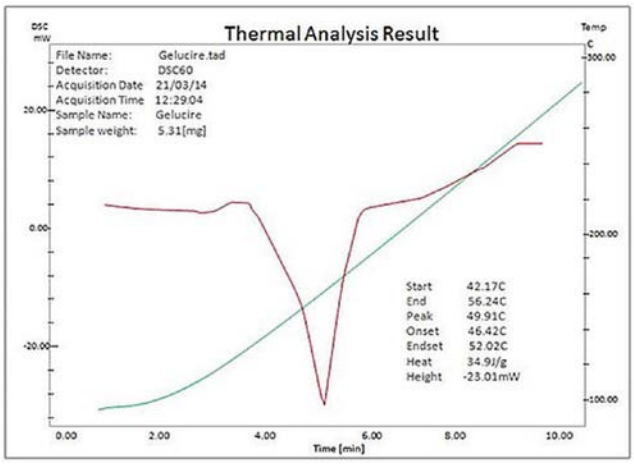

Figure 3B:DSC spectra of Gelucire 50/13.

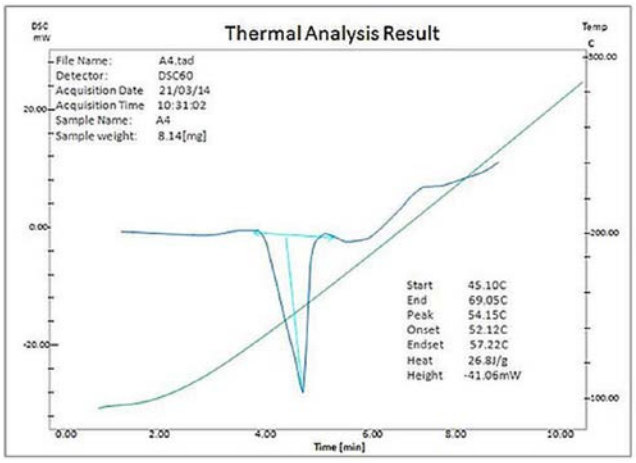

Figure 3C: DSC spectra of Etodolac melt dispersion granules A4.

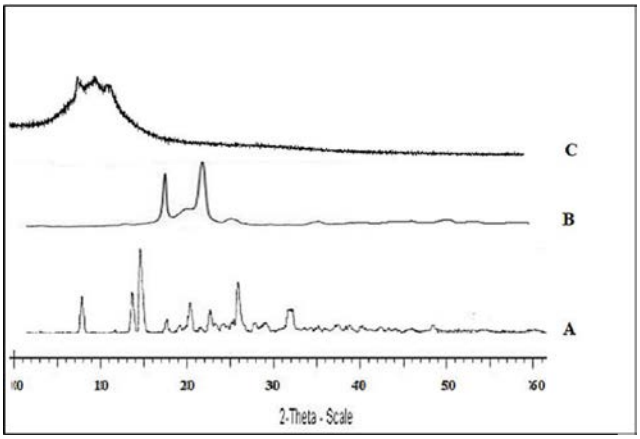

Figure 4: XRD images of A-Etodolac, B-Gelucire50/13 and C-Melt dispersion Granules of Etodolac.

corresponding to melting temperature of Gelucire 50/13. The melt granulated dispersion have latent heat of fusion (ΔH_{fus}) 26.8J/g. The decrease in enthalpy and disappearance of etodolac characteristic endothermic peak in melt granulated dispersion revealed reduction in crystallinity as well as dispersion of etodolac in melt dispersion granules.

Powder XRD study

X-ray diffraction patterns of etodolac, Gelucire50/13 and melts dispersion granules (A4) were studied to find the changes in crystallinity of etodolac on loading. Diffractogram of etodolac showed (Figure 4) intense peak at diffraction angle 15θ with narrow baseline. Gelucire 50/13 showed sharp peaks diffraction angle at 16θ and 22θ. X-ray diffractogram of optimized melts dispersion granules (A4) clearly indicates that disappearance of etodolac and Gelucire50/13 intense peaks and broadening of the base line. The disappearance

of major peaks of etodolac in melts dispersion granules (A4) indicated reduction in crystallinity of drug. Hence the crystalline drug was successfully converted to amorphous by the hydrophilic binder Gelucire 50/13.

Preparation of Etodolac tablet

Drug loaded melt dispersion granules based tablets were successfully prepared using 16-station rotary tablet compression machine (CADMACH, Ahemdabad). Initially tablets were adhered to the upper punch however incorporation of microcrystalline cellulose along with magnesium stearate overcome this difficulty. Sublimating agents containing tablets were weighed before and after sublimation.

Evaluation of tablets

The hardness of tablet for F0 to F8 was found in the range of 4.71±0.26 to 4.13±0.28 kg/cm^2. This rendering that, required compressibility was imparted due to Aerosil 200. After sublimation of F5-F8, the hardness was decreased and found in the range of 4.03±0.29 kg/cm^2 to 4.27±0.22 (Table 3A), due to formation of channels in the activated tablets hardness was decreased even though fair hardness values observed. The thickness of melt dispersion granulated tablet of etodolac tablets for F0 toF8 was found to be within the range of 5.0±0.11 to. 5.04±0.112 mm. Etodolac tablets for F0 to F8 formulation showed weight variation within the range of 899.2±0.72 to 900.1±0.65. This indicates that flowability is good. The weight variation after sublimation found to be 776±0.38-798±0.39 (Table 3B). Friability of formulations F0 to F8 ranges from 0.21±0.01 to 0.31±0.10. All formulation revealed the percent friability less than 1%, which specified good mechanical strength. Disintegration time of etodolac melt granulated tablet was found to be 51±1.31-368±1.52 sec. In case of tablets prepared by sublimation (F5, F6, F7 and F8) have capacity to disintegrate the formulation faster than other formulations containing superdisintegrants (F1, F2, F3 and F4). The lowest disintegration time for F8 which was 51±1.31 sec gives faster release than other formulations. Post compression study parameters data was subjected for one way ANOVA analysis *p* values were found to be within 0.05 indicates significance in the experimental data.

Determination of Content Uniformity

Percent content of etodolac in melt granulated tablets of F0 to F8 formulation were found to be in the range of 99.8±0.52% to 100.3±0.51% (Table 3A). Drug content estimation data for all the formulations was found to be within prescribed limits (NLT 98% And NMT 102%, B.P.) This is the sign of homogeneous

Table 3A: Post compression evaluation of Melt dispersion granulated Tablet of Etodolac (*n*=3).

Parameters	Formulation code								
	F0	F1	F2	F3	F4	F5	F6	F7	F8
Hardness (kg/cm^2)	4.58±0.28$^{\#}$	4.23±0.28$^{\$}$	4.13±0.28$^{\#}$	4.19±0.28$^{\$}$	4.35±0.28$^{\#}$	4.67±0.22$^{\Psi}$	4.25±0.23$^{\#}$	4.71±0.26$^{\#}$	4.21±0.26$^{\Psi}$
Thickness (mm)	5.0±0.11$^{\Psi}$	5.01±0.1$^{\#}$	5.04±0.005$^{\#}$	5.00±0.11$^{\#}$	5.03±0.11$^{\$}$	5.0±0.17$^{\Psi}$	5.02±0.112$^{\$}$	5.01±0.10$^{\Psi}$	5.04±0.26$^{\Psi}$
Weight variation	900.1±0.65$^{\Psi}$	899.3±0.72$^{\$}$	899.5±0.75$^{\Psi}$	900±0.72$^{\$}$	899.7±0.63$^{\Psi}$	900.2±0.76$^{\#}$	897.6±0.62$^{\$}$	900±0.52$^{\#}$	899.8±0.6$^{\Psi}$9
Friability (%)	0.21±0.01$^{\Psi}$	0.22±0.04$^{\#}$	0.27±0.03$^{\Psi}$	0.31±0.10$^{\Psi}$	0.23±0.05$^{\#}$	0.25±0.01$^{\Psi}$	0.30±0.07$^{\#}$	0.21±0.02$^{\Psi}$	0.28±0.02$^{\Psi}$
Disintegration Time (sec)	368±1.52$^{\Psi}$	77±1.39$^{\Psi}$	68±1.00$^{\Psi}$	64±1.21$^{\#}$	59±1.13$^{\Psi}$	60±1.09$^{\Psi}$	59±1.34$^{\#}$	54±1.28$^{\Psi}$	51±1.31$^{\Psi}$
Drug content %	99.8±0.52$^{\Psi}$	99.9±0.24$^{\$}$	100.3±0.51$^{\Psi}$	100±0.28$^{\$}$	99.9±0.33$^{\Psi}$	99.9±0.20$^{\Psi}$	100.1±0.28$^{\$}$	100.2±0.24$^{\Psi\Psi}$	99.9±0.33$^{\Psi}$

(*n* = 6) *Values represent Mean ± SD, ($^{\#}p < 0.01$, $^{\$}p < 0.02$, $^{\Psi}p < 0.05$)

Table 3B: Post compression parameters of melt dispersion granulated tablet of Etodolac after sublimation. (*n*=3).

Parameter	Formulation code			
	F5	F6	F7	F8
Hardness (kg/cm²)	4.13±0.38$^{\psi}$	4.03±0.29$^{\$}$	4.27±0.22$^{\psi}$	4.06±0.32$^{\$}$
Weight variation	790±0.40$^{\#}$	776±0.38$^{\$}$	798±0.39$^{\#}$	785±0.40$^{\psi}$

(*n* = 6) *Values represent Mean ± SD, ($^{\#}p < 0.01$, $^{\$}p < 0.02$, $^{\psi}p < 0.05$)

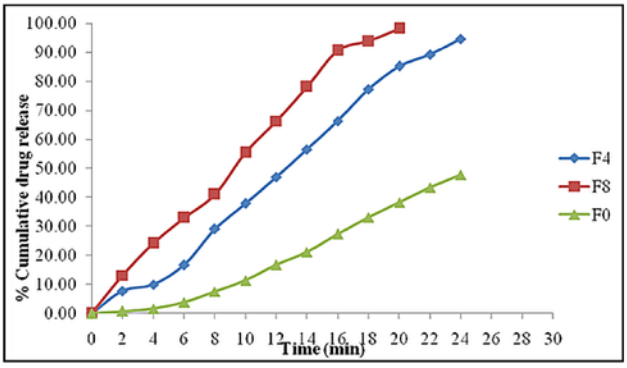

Figure 5: *In vitro* Dissolution Profile of Formulation F0, F4 and F8.

mixing of etodolac in granules. Content uniformity data was subjected for one way ANOVA analysis *p* values were found to be within 0.05 indicated significance in the experimental data.

In-vitro dissolution study

The *in -vitro* dissolution behavior of etodolac melt granulated tablet studied in HCl buffer pH 1.2. *In vitro* dissolution test formulation F0 to F8 showed cumulative % drug release of 47.72%, 90.70%, 91.96%, 92.28%, 94.64%, 93.77%, 94.01%, 96.65% and 98.14% respectively. The *in -vitro* release profile revealed that all Etodolac formulation show higher drug release than formulation F0. Formulation F0 showed least release at the end of 24 min that is 47.72%, this was due to poor disintegration of tablet. Further the addition of superdisintegrant and sublimating agents in tablet (F1-F8) showed marked decrease in disintegration time. The formulation containing superdisintegrants (SSG and CCS) in different concentration showed cumulative percent drug release of 90.70%, 91.96%, 92.28 % and 94.64% respectively at the end of 24 min. Once the concentration of superdisintegrant increases the cumulative drug release elevates. The CCS at concentration 6% (F4) gives highest release 94.64% than CCS 4% (F3) and SSG (F1, F2). But in case of formulations F5-F8 containing camphor and menthol showed increased % cumulative drug release and gave highest release within 20 min. The percent cumulative drug release in F8 formulation containing menthol (7%) was 98.14% and which is significant. Although formulation containing superdisintegrant the release was higher, the formulation containing sublimating agent menthol (F8) gives highest release than CCS (F4) in less time. The cumulative drug release from formulation F0, F4 and F8 is depicted in Figure 5. The main factor behind the increased drug release was porosity formed in the tablet after sublimation. From the above data, the formulation F8 containing menthol (7%) gives highest percent cumulative drug release within 18-20 min (Figure 5). As the concentration of sublimating agent increased the highly porous structure formed which gives faster disintegration and hence enhanced dissolution within less time. The drug surface accessible for dissolution can be extremely increased due to surface coating material Aerosil200 which enhances the dissolution rate also. Thus formulation F8 is optimized formulation with improved dissolution profile.

Mean dissolution time, DE10 and DP10 of Etodolac melt dispersion granulated tablets are given in (Table 4). The mean dissolution time for optimized tablet formulation F8 is 8.90 min and is less as compared to all formulations. The formulation F8 is having DE10 28.25% and percent drug dissolved at 10 min (DP10) was maximum for F8; 55.45%. Dissolution study data was subjected for one way ANOVA analysis *p* values were found to be within 0.05 indicates significance in the experimental data.

CONCLUSION

The present work concludes that the melt dispersion granule technique with surface adsorption and use of sublimating agent provided promising results. Hence it can be a potential approach to improve the dissolution rate of poorly soluble etodolac. The etodolac tablets formulated with sublimating agent camphor have enhanced dissolution profile with suitable tableting properties. *In vitro* dissolution studies indicated the dissolution improvement from etodolac tablet. The XRD along with DSC studies revealed decrease in crystallinity and this factor is contributing towards dissolution rate improvement for Etodolac.

ACKNOWLEDGEMENT

We are thankful to Ipca laboratories, Mumbai and Gattefosse India for providing gift samples of etodolac and Gelucire 50/13 respectively.

Table 4: Mean Dissolution Time (MDT), DE_{10} and DP_{10}.				
Sr.no.	Formulation code	MDT(min)	DE_{10} (%)	DP_{10} (%)
1	F0	12.82±0.87$^{\$}$	9.91±1.1$^{\Psi}$	11.37±1.12$^{\#}$
2	F1	13.87±0.79$^{\#}$	13.07±0.98$^{\$}$	28.47±0.87$^{\$}$
3	F2	13.15±0.871$^{\#}$	13.66±0.86$^{\Psi}$	30.21±0.81$^{\Psi}$
4	F3	12.32±0.82$^{\#}$	15.90±0.92$^{\$}$	35.22±0.789$^{\#}$
5	F4	11.95±1.1$^{\#}$	16.66±0.86$^{\$}$	37.89±0.691$^{\$}$
6	F5	9.65±0.98$^{\Psi}$	24.54±0.93$^{\Psi}$	46.04±0.861$^{\Psi}$
7	F6	9.13±0.93$^{\Psi}$	25.83±0.97$^{\Psi}$	48.57±0.741$^{\#}$
8	F7	9.18±0.86$^{\Psi}$	26.64±0.89$^{\$}$	51.51±0.862$^{\Psi}$
9	F8	8.90±0.96$^{\Psi}$	28.25±1.12$^{\Psi}$	55.45±0.95$^{\$}$

(n = 6) *Values represent Mean ± SD, ($^{\#}p < 0.01$, $^{\$}p < 0.02$, $^{\Psi}p < 0.05$)

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

GIT: Gastro Intestinal Tract; **BCS:** Biopharmaceutical Classification System; **API:** Active Pharmaceutical Ingredient; **PEG:** Polyethylene glycol; **HLB:** Hydrophilic Lipophilic balance; **FTIR:** Fourier Transmission Infra-Red; **DSC:** Differential Scanning Calorimetry**; CCS:** Cross Carmellose Sodium; **SSG:** Sodium Starch Glycolate; **MDT:** Mean Dissolution Time.

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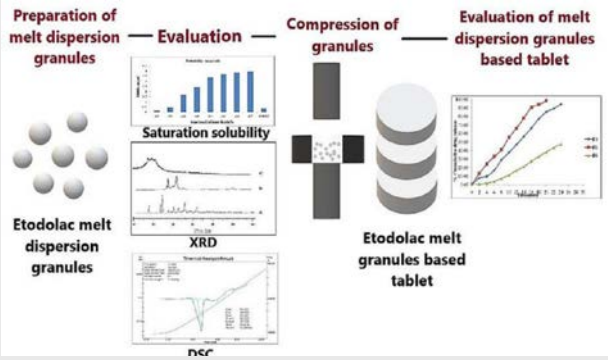
PICTORIAL ABSTRACT



SUMMARY

Etodolac is a poorly water soluble drug and needs dissolution enhancement to improve its therapeutic efficacy. In this research work, dissolution of etodolac is increased by using hydrophilic meltable carrier Gelucire50/13. Incorporation of superdisintegrants and sublimating agents increased drug release rate. Sublimating agent i.e. menthol (7%) showed fast disintegration of tablet. Formulation F8 showed best result for *in-vitro* dissolution study. The tableting properties of all formulation F1-F8 were also increased. Thus melt granulation could be acceptable avenue to improve dissolution and tableting properties of etodolac.

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