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Enhancement of dissolution rate of indomethacin by kollicoat IR based solid dispersions

[1]S. H. Shirke[*], [2]A. S. Shete and R. C. Doijad

[1]Department of Pharmaceutics, Satara College of Pharmacy, Satara
[2]Research Group Department of Pharmaceutics and Quality Assurance, Shree Santkrupa College of Pharmacy, Ghogaon, Karad, MS

ABSTRACT

Amorphization is a commonly used method to enhance the dissolution of poorly water-soluble drug. In this study Kollicoat IR , a new pharmaceutical excipient developed as a coating polymer for instant release tablets, was evaluated as a carrier in solid dispersions of Indomethacin. The solid dispersions of indomethacin with kollicoat IR were prepared at ratio 1:1 by different methods such as co-grinding, solvent drop co grinding, kneading and solvent evaporation method to achieve dissolution rate enhancement. Fourier transform infra red spectroscopy, Differential scanning calorimetry, X-ray powder diffraction and nuclear magnetic resonance spectroscopy were used to evaluate the interaction or miscibility between the drug and the carrier. The pharmaceutical performance was evaluated by dissolution experiments, performed in 1 part phosphate buffer pH 7.2 and 4 parts water. The X-ray diffractogram and nuclear magnetic resonance spectroscopy indicates indomethacin transformed from the crystalline state to the amorphous state. Differential scanning calorimetry revealed molecular dispersion of drug within polymer as disappearance of characteristic melting point of crystalline drug. In stability study, amorphous IMC in the solid dispersion did not crystallize under storing room temperature for 6 month due to antiplasticizing effect of polymer. The transformation of indomethacin from crystalline to amorphous state by using Kollicoat IR is considered a promising way to improvement of drug dissolution.

Key words: Kollicoat IR, dissolution rate, amorphous, kneading.

INTRODUCTION

Indomethacin is non-steroidal anti-inflammatory drug[NSAIDs][1] used to reduce pain or swelling involved in osteoarthritis, rheumatoid arthritis, bursitis, tendinitis, gout, ankylosing spondylitis, and headaches[2].Given the fact that its permeability is adequate, Indomethacin is a class II drug, according to the biopharmaceutical classification system. A severe limitation in the oral bioavailability of class II compounds is that dissolution takes longer than the transit time through their absorptive sites, resulting in incomplete bioavailability [3]. Drugs with dissolution limited oral absorption might benefit from a larger solid–liquid contact surface area and an increase in saturation solubility. This is well described in the following equation, which is a modification of the well-known Noyes–Whitney relation [4]

$$dM/dt = AD. (Cs - C) /h$$

Where, d*M*/d*t* is dissolution rate,
A is Specific surface area of the drug particle,
D is diffusion coefficient,
h is diffusion layer thickness,
C is saturation solubility and

C t is drug concentration at time *t*.

Both principles form the rationale for the use of solid dispersions, a possible pharmaceutical strategy that can result in increased solubility and dissolution rate. The potential of solid dispersion technology in improvement of bioavailability and therapeutic activity of hydrophobic agents has been well established due to simplicity of preparation, ease of optimization and reproducibility. The term solid dispersion refers hydrophobic drug is molecularly dispersed into hydrophilic carrier at solid state, usually to enhance bioavailability [5]. The presence of the carrier improves the contact between the drug and the dissolution medium and inhibits the aggregation and agglomeration. Due to particle size reduction the drug is molecularly dispersed in the carrier. Compared to solid dispersions with separate amorphous drug clusters, these systems have a higher physical stability due to the antiplasticizing effect and protection against recrystallization from the surrounding polymer [6].Both in terms of dissolution as in terms of stability the solid solutions are favorable systems. Kollicoat IR was employed as carrier in preparation of solid dispersions. It is graft copolymer of polyvinyl alcohol (75% units) and polyethylene glycol (25% units). Its solubility is 40% (w/w) in aqueous systems and 25% (w/w) in a 1:1 ethanol–water mixture; the solubility in non-polar solvents is low [7]. It exhibit good wetting behavior by reducing the surface tension of water, this makes aqueous solution easy to spray. It is an interesting polymer to be used as a carrier for the formulation of solid dispersions. As it is hydrophilic and non-ionic, its solubility does not change along with the gastrointestinal tract [8]. It is slightly surface active [9], which can be useful to maintain super saturation of poorly soluble drugs in the gastrointestinal tract.

Large number of studies has been carried out on solid dispersions but still there is need to explore new carrier material and stability of solid dispersions. In order to contribute in the search of new carriers, we have investigated the potential of Kollicoat IR as a polymeric carrier in the formulation of solid dispersions of Indomethacin.

The objective of the present study was to enhance dissolution rate of indomethacin using solid dispersion with Kollicoat IR. To study the possible interactions between indomethacin and Kollicoat IR. To carry out the stability of amorphous indomethacin in solid dispersion.

MATERIALS AND METHODS

A gift sample of indomethacin was received from Alembic pharma Ltd. (Baroda, India) Kollicoat IR was received from Lupin Pharmaceuticals, (Pune, India).

Preparation of solid dispersions:
Solid dispersions and physical mixture of indomethacin with Kollicoat IR were prepared at (1:1) ratio by various methods (Table 1).

2.1Physical mixtures:
Indomethacin and Kollicoat IR were accurately weighed, pulverized and mixed thoroughly by light trituration for 5 min in a mortar. The mixture was passed through a sieve no-60.

2.2 Kneading method*:*
A required amount of Kollicoat IR and indomethacin were taken in a glass mortar. The mixture was kneaded thoroughly with a glass pestle by using ethanol for 30 minutes. The mixture was kept for drying in a desiccator. The hardened mixture was powdered in a mortar, sieved through a 60-mesh screen, and stored in screw-cap vial at room temperature [10].

2.3 Co grinding method:
Amount of Kollicoat IR® and indomethacin were taken in a glass mortar. The mixture was triturated for 15 minutes .Prepared mixture stored in screw-cap vial at room temperature.

2.4 Solvent drop co grinding method:
Accurately weighed drug and polymer were taken in a glass mortar. The mixture was triturated for 15 minutes by using 1-2 drops of ethanol. Prepared solid dispersion stored in screw-cap vial at room temperature.

2.5 Solvent evaporation method:
Solid Dispersions of indomethacin were prepared by common solvent method [3, 9] employing ethanol as solvent. The weighed quantities of indomethacin and Kollicoat IR® were dissolved in the corresponding solvent in a round bottom flask to get a clear solution. The resulting mixture was stirred for one hour and evaporated at temperature 40-

45^0C on water bath until nearly dry mass was obtained. The mass obtained was further dried at 50°C for 4 h in an oven. The product was crushed, pulverized and shifted through mesh no-60[3, 9].

TABLE 1: FORMULATIONS OF INDOMETHACIN SOLID DISPERSION

Formulation code	Drug: Polymer	Method
F1	1:1	Physical mixture
F2	1:1	cogrinding
F3	1:1	Solvent Drop
F4	1:1	kneading
F5	1:1	Solvent evaporation

EVALUATION OF SOLID DISPERSIONS

3.1 Percentage yield:

The prepared solid dispersions and physical mixtures were weighed after processing and product yield was calculated by using following equation:--

$$Y = (a/b+c) \times 100$$

Where, a -weight of solid dispersion
b -weight of Indomethacin taken
c -weight of polymer (Kollicoat IR) taken for solid Dispersions and physical mixture

3.2 Drug content determination:

Amount of drug present in the solid dispersions and physical mixtures was determined by sampling 10mg of solid dispersions and physical mixture in 100 ml of volumetric flask. To this 1 part of phosphate buffer pH 7.2+ 4 parts of water was added and the flask was shaken for 10 min, final volume was made up to 100mL with same. From that solution 1mL was transferred to another volumetric flask of 10 ml and volume was made with same. The amount of drug present was analyzed spectrophotometrically at 320 nm and indomethacin content was calculated [11].

3.3 Saturation solubility study:

The solubility of pure indomethacin, physical mixture and solid dispersions was estimated in distilled water,0.1 N HCL, Phosphate buffer pH 7.2+water.For this saturated solution of drug and formulations were prepared in 10 ml of each solvent. To facilitate maximum solubilization of drug in the solvent at room temperature it was kept in water bath shaker for 24 h at 25^0 C to achieve equilibrium. The solutions were observed for a clear transparent solution. The amount of drug present in the solvents was estimated using UV visible spectrophotometer at 320 nm after appropriate dilutions [12]. The study was performed in triplicate (n =3).

3.4 In-vitro dissolution studies:

Dissolution studies of indomethacin in powder form, Solid dispersions and physical mixture were performed by using the (USP) model digital tablet dissolution test apparatus-2 (DBK- Dissolution rate test apparatus.) at the paddle rotation speed of 100 rpm in 750 ml mixture of 1 part phosphate buffer pH 7.2 and 4 part water. The solid dispersions and Physical mixture equivalent to 50 mg of indomethacin was weighed using a digital balance and added into the dissolution medium. At the specified times 5 ml samples were withdrawn by using syringe filter (0.45µm) and then assayed for indomethacin content by measuring the absorbance at 320 nm using the UV-Visible spectrophotometer (Jasco V_{530} Japan) . Fresh medium (5ml), which was prewarmed at 37^0C, was replaced into the dissolution medium after each sampling to maintain its constant volume throughout the test.

3.5 Fourier transform infrared spectroscopy:

Fourier-transform infrared (FTIR) spectra were obtained by using an FTIR spectrophotometer (Jasco 410, Japan). Samples were mixed with potassium bromide and compressed into discs using hydraulic press. The IR spectra in absorbance mode were obtained in the spectral region 4000-400 cm^{-1}. The FTIR spectra of pure drug, physical mixture and solid dispersions were compared to check any interactions between the drug and polymer or change in the positions of the functional group of the drug.

3.6 Differential scanning calorimetry:

The thermal behavior of Indomethacin, Kollicoat IR, Physical mixture and Solid dispersions were studied using TA instrument (SDT 2960, USA). Accurately weighed samples were placed in standard aluminum pans and covered with a pierced lid. Dry nitrogen was used as the purge gas, at a flow rate of 100mL/min. The thermo grams were obtained by heating the samples at a rate of 10°C/ min from 30 °C temperature to 300 °C.

3.7 Powder X-ray diffraction studies:
XRD were carried out to determine the physical state of the drug in the solid dispersion system. The X-ray diffraction patterns were obtained by using D2 Phaser diffractometer. The radiation used was generated by a Cu Ka source fitted with a nickel filter, operated at voltage of 45 kV, current 40mA.The samples were analyzed in the angle range (2θ) of 5^0-90^0. All XRD spectra were compared.

3.8 Nuclear Magnetic Resonance Spectroscopy:
^{1}H NMR spectra of IND and SD prepared by co-grinding method were recorded using a Mercury plus 300 MH_z NMR spectrophotometer (Japan) at ambient temperature. The spectrometer was operated at 100 MHz using 5mm Auto switchable probe with PFG. The measurement conditions were as follows: spinning rate 5 kHz, contact time 1msec, acquisition time 25 ms, solvent used was DMSO.

3.9 Stability Studies of Solid Dispersions:
The prepared solid dispersions charged for stability studies. The samples were kept for stability studies at ambient temperature for period of 6 months. The samples were kept in glass vials sealed with rubber plugs. Stored solid dispersions were withdrawn at 180 days and analyzed for physical change, drug content, dissolution studies, FTIR studies, PXRD studies.

RESULTS AND DISCUSSION

Solid dispersions of indomethacin were prepared by using polymer Kollicoat IR®. In the present work five formulations were prepared by using five different methods at 1:1 (indomethacin: Kollicoat IR) ratio and their composition is shown in (Table 1)

4.1 % Drug Content and % Yield:
The drug content was determined to evaluate the homogeneity of distribution of drug in physical mixtures and solid dispersions and drug yield was determined to evaluate any loss of drug that occurred during the preparation of mixtures. The results revealed drug content values in the range of 95.8-98.80 % w/w indicating homogenous distribution of the drug in prepared mixtures. The production yield was found satisfactory and ranged from 95.50-98.50% for solid dispersions. The results of % drug content and % drug yield are shown in (Table 2**)**

TABLE 2: EVALUATION OF SOLID DISPERSIONS

	%DC	% Y	%DR (at end60 min)
F1	95.88±0.09	95.50±0.05	41.47±0.02
F2	97.20±0.02	98.00±0.06	80.86±0.01
F3	98.80±0.01	97.00±0.066	76.08±0.05
F4	98.74±0.020	97.00±0.11	56.85±0.03
F5	96.86±0.024	98.50±0.035	64.43±0.035

Indomethacin solid dispersions bearing different FC= formulation code F1, F2, F3, F4, F5 were evaluated for %DC= drug content, %Y= drug yield, %DR = cumulative drug released. All values are mean ±standard deviation of three determinations.

4.2 Solubility Study:
The solubility studies of drug, physical mixture and solid dispersions were carried out in different solvents like water, 0.1 N HCL, 1 part phosphate buffer pH 7.2 + 4 parts water. The results of solubility studies of physical mixture and solid dispersions prepared by various methods revealed that there was slightly increase in solubility of physical mixture and significant improvement in the solubility of solid dispersions in all solvents as compared to pure indomethacin but drastic improvement of solubility in 1-part phosphate buffer pH 7.2 + 4-parts water. This improvement in drug solubility in formulations may be due to cosolvensy effect of carrier, changes in the crystal forms, structure and surface modification with hydrophilic polymer Kollicoat IR. The hydrophilic carrier may interact with drug molecule by hydrogen bonding or other types of bonding and this was likely cause for the formation of weakly soluble complexes [14].The results of the solubility study of solid dispersions, physical mixtures and drug mentioned in (Table 3) and (fig.1).

TABLE 3: SATURATION SOLUBILITY OF IND AND SOLID DISPERSIONS IN DIFFERENT SOLVENTS

FC	Solubility µg/ml		
	0.1 N HCL	Pb 7.2+ DW	Distilled water
Pure IND	6.34±0.03	15.20±0.01	10.26±0.02
F1	12.55±0.01	48.24±0.14	36.17±0.03
F2	22.81±0.01	94.78±0.012	41.64±0.039
F3	20.76±0.02	87.28±0.09	41.34±0.04
F4	20.65±0.04	89.28±0.06	41.17±0.01
F5	17.92±0.018	80.93±0.03	41.09±0.03

Solubility study of drug and solid dispersions was carried out for 24 hrs in 0.1 N HCL, 1 part Phosphate buffer pH 7.2+ 4 parts water and Distilled water. All values are mean ± standard deviation of three determinations.

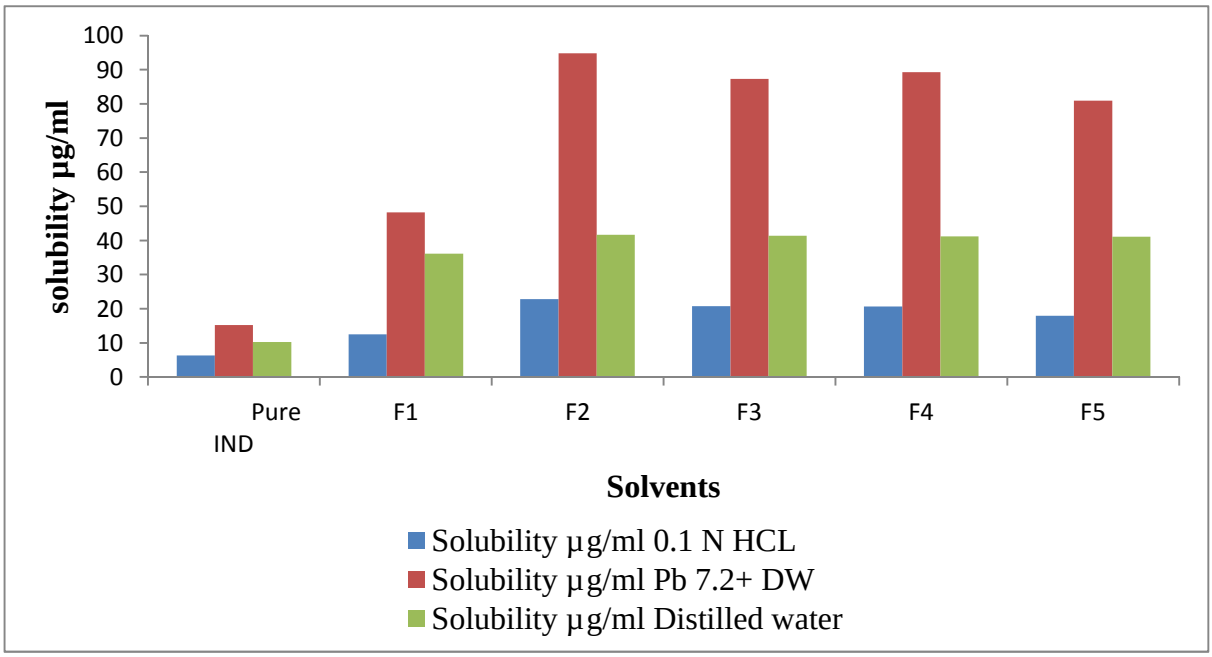

Fig. 1: Saturation solubility of IND and their solid dispersions in different solvent

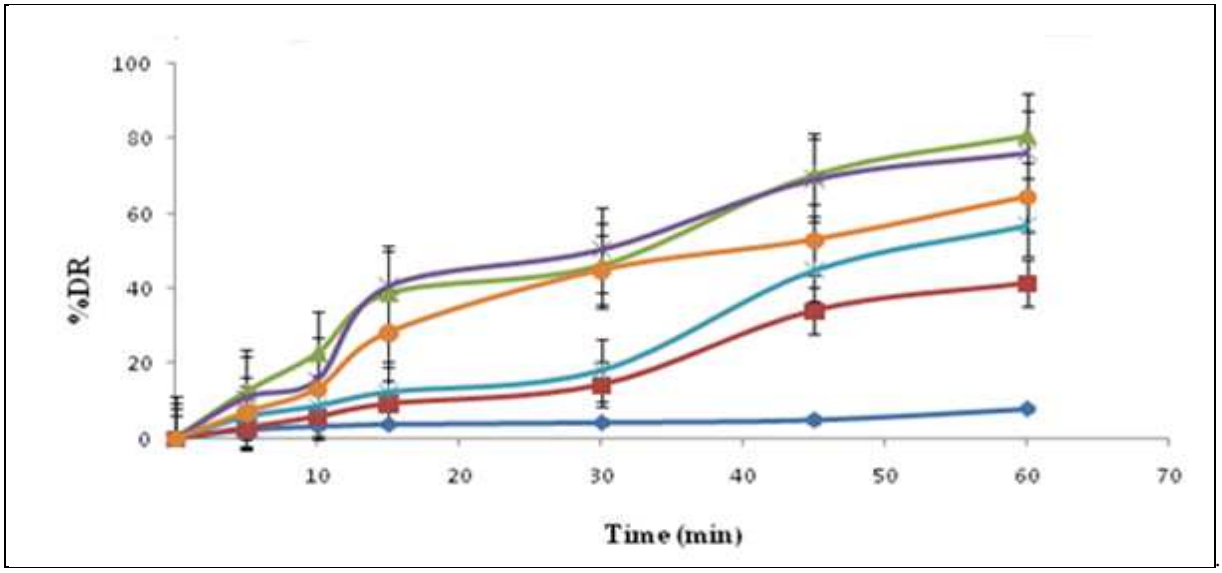

Fig. 2: Cumulative Percent drug Release of pure indomethacin and its solid dispersions with time
Cumulative drug release was measured *in- vitro* over a period of 1 hr from solid dispersionsprepared with kollicoat IR by using various methods.(Pure IND),(Physical Mixture),(Cogrinding),(Solvent drop cogrinding),(Kneading)(Solvent evaporation)

4.3 In-vitro dissolution studies:

The results of dissolution studies for individual samples (pure indomethacin, physical mixture and solid dispersions) over the period 60 min were noted. Cumulative percent drug released after 60 min was 41.47%, 80.86%, 76.08%, 56.85%, 63.43% for F-1 to F-5 respectively and 8.08% in 60 min for pure drug as shown in (fig.2). Dissolution studies revels that there is marked increase in dissolution rate of indomethacin from all solid dispersions as compare to pure indomethacin. The improvement of dissolution rate was possible due to several factors such as: a) the strong hydrophilic character of Kollicoat IR, which improves the water penetration and the wettability of the hydrophobic indomethacin and maintain supersaturation of drug b) the molecular dispersion of indomethacin in Kollicoat IR

leads to partial miscibility, improving the hydrophilic characteristics of the drug substances through interaction within the polymer, c) reduction in particle size resulting increased surface area [15].

4.4 Fourier transform infrared spectroscopy:

The IR spectra of solid dispersions and physical mixture were compared with spectrum of indomethacin (fig.3). The IR spectrum of plain indomethacin showed characteristic peaks at 1714.87 cm^{-1} and 1690.80cm^{-1} due to c=o stretching,1598.28 cm^{-1}due to aromatic c≡c stretching, 1453.04 cm^{-1} due to O-CH_3 deformation,1229.34cm^{-1} due to C-O stretch and OH deformation[1]. The new peaks observed in the range of 2500-3000 cm^{-1} indicate OH stretching of carboxyl group. The broad peaks observed in the range of 3500-370034cm^{-1} indicates O-H stretching suggesting hydrogen bonding [9]. Spectra of all solid dispersions appear simple as compared to IND spectrum. These results indicate the crystalline structure of indomethacin in solid dispersions with Kollicoat IR changes to amorphous form and this is due to IND molecules interact with Kollicoat IR through hydrogen bonding and make eutectic mixtures[16]. These results were confirmed further by DSC and PXRD study.

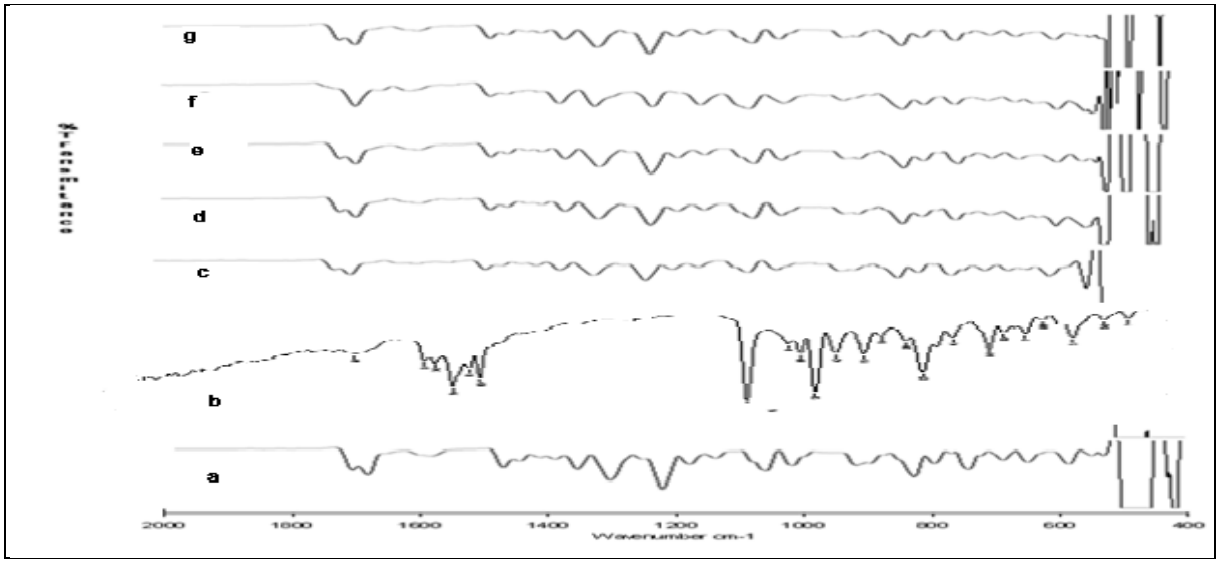

Fig.3: Comparative FTIR pattern of pure drug, physical mixture and IND- Kollicoat IR solid dispersions prepared by various methods
(a) Pure IND, (b) Kollicoat IR (polymer), (c) Physical mixture (d) Co-grinding, (e) Solvent drop co-grinding, (f) Kneading. (g) Solvent evaporation.

4.5 Differential scanning calorimetry:

Differential scanning calorimetry (DSC) revealed complex structure of solid dispersions. DSC thermograms are obtained for IND, Kollicoat IR and solid dispersions. DSC curves of pure drug and formulations were compared (fig.4). Pure indomethacin has showed well defined endothermic peak (T_m) at 161.03^{0}c corresponding to the melting point of crystalline drug. Two melting endotherms were observed in all formulations. The physical mixture and solid dispersions showed first melting endotherms at 150.34^{0}c, 152.60^{0}c, 151.93^{0}c, 144.26^{0}c, 152.30^{0}c with reduction in peak areas and melting points. Depression of melting point and different than drug and individual polymer thus confirming the formation of new phase. Physical mixture and solid dispersions showed melting points lower than the drug and polymer. Lowering of melting points was due to the breaking of bonds, disordered and non randomized structure of molecule. It leads to lower activation energy to reach the melting points. The broad, less sharp peaks with reduction in melting point of indomethacin in solid dispersions shows decrease in the gradual dissolution of the drug in the polymer during the DSC heating ramp [17]. Second endotherm in all formulation due to chiral nematic mesophase of glassy indomethacin. The results of DSC studies indicate heating partially crystallized glassy indomethacin leads to formation of stable polymorph [18]. First melting endotherms were due to kollicoat IR which indicate some sort of crystal part converted into amorphous form. Amorphous state indicating the drug was molecularly dispersed within carrier.

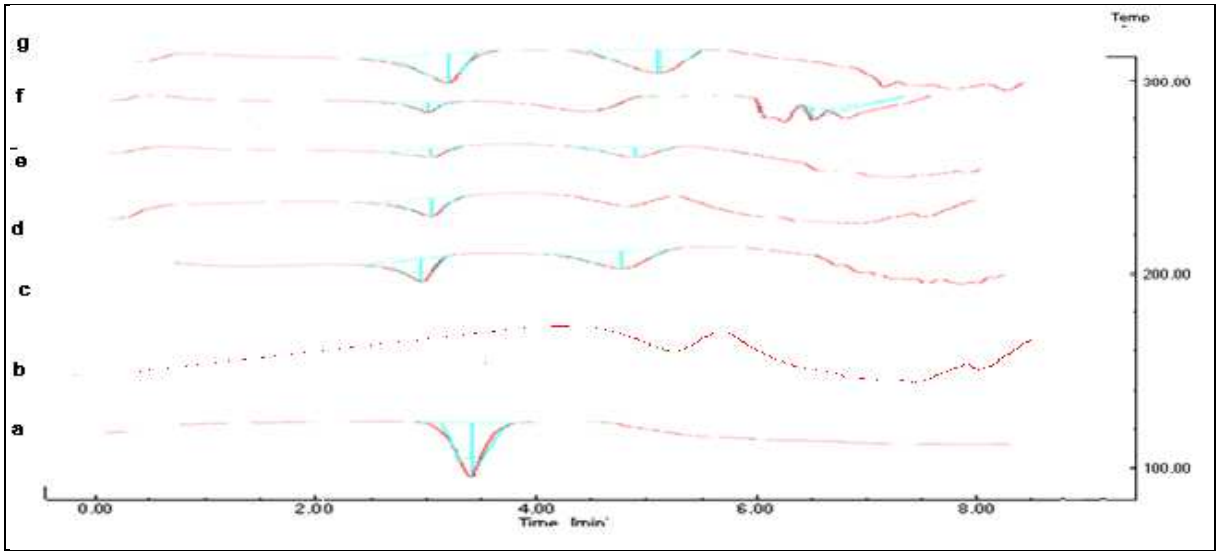

Fig.4: Comparative DSC pattern of pure drug, physical mixture and IND- Kollicoat IR solid dispersions prepared by various methods
(a) Pure IND, (b) Kollicoat IR (polymer), (c) Physical mixture (d) Co grinding, (e) Solvent drop cogrinding, (f) Kneading, (g) Solvent evaporation.

4.6 Powder X-ray diffraction studies:

The PXRD patterns of the pure drug, polymer and solid dispersions were compared. (fig.5). The PXRD scan of plain indomethacin showed intense peak at 11.62^0 and $23.79^0(2\theta)$ with peak intensity 2330, 2314 respectively indicating its crystalline nature. X-ray diffractogram of Kollicoat IR shows a characteristic broad reflection centered at 11.2^0 (2θ) indicating its semi crystalline nature. Diffractograms of solid dispersion F1-F5 showed all principal peaks from indomethacin which were broader, fewer and less intense, which suggested the portion of drug has been converted into amorphous form. The X-ray diffraction findings also suggest that some portion of drug still exist in the same crystalline structure of but the relative reduction of diffraction intensity of drug in solid dispersions at specific angles suggests that the drug partially converted into amorphous form [18].

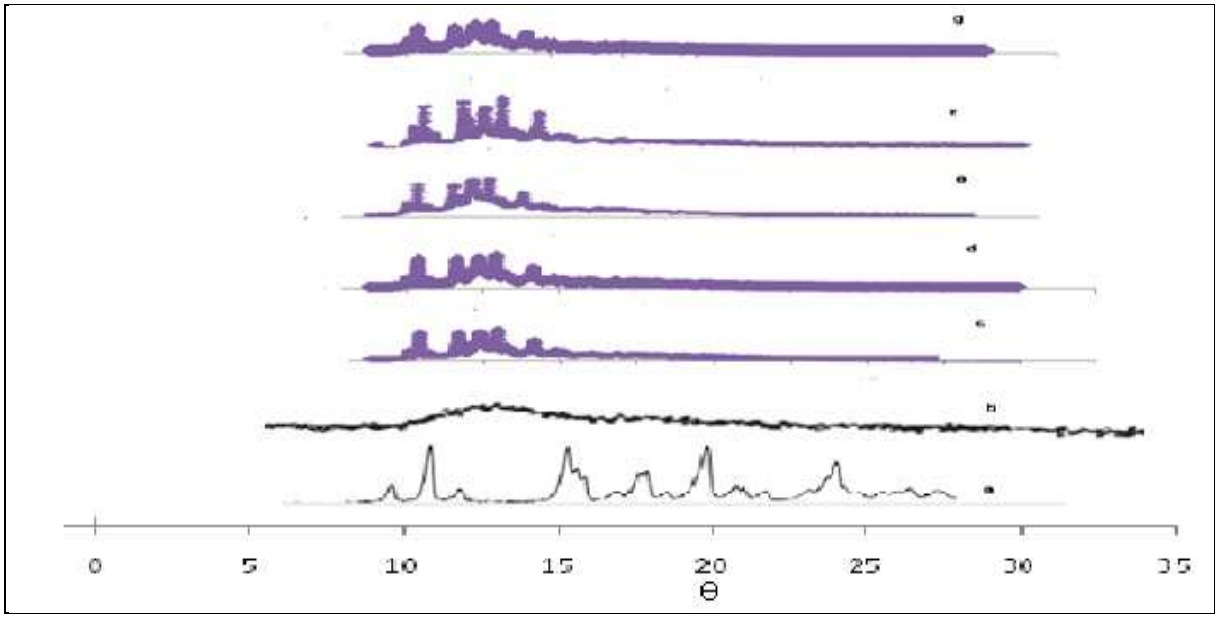

Fig.5: Overlay of comparative XRPD Diffractograms of pure drug, physical mixture and IND- Kollicoat IR solid dispersions prepared by various methods.
(a) Pure IND, (b) Kollicoat IR (polymer), (c) Physical mixture (d) Cogrinding, (e) Solvent drop cogrinding, (f) Kneading, (g) Solvent evaporation.

4.7 Nuclear Magnetic Resonance Spectroscopy:

Solid-state NMR was performed to detect the interaction between drug and polymer in solid dispersion (fig. 6). In the ^{1}H NMR spectra of IND the aromatic proton allocated at 6.69 -7.69, proton of methyl group allocated at 2.21-2.50, protons of CH_2COOH and OCH_3 located at 3.36- 3.66 and 3.75-4.25 respectively [1]. Whereas in solid

dispersion corresponding signals appeared with decrease in peak height at 6.68-7.692 for aromatic protons,2.20-2.50 for methyl protons 3.407 -3.64 for CH_2COOH and 3.75- 4.25 for OCH_3 respectively which reveals that there is no deteriorate effect of polymer on drug but new peaks were observed in the range of 3.3- 4.4 ppm indicative of OH protons. Change in peak height, peak area and new peaks in spectra suggest drug polymer interaction through hydrogen bonding .The chemical shifts is very strongly affected by hydrogen bonding. OH signals move downfield in hydrogen bonding solvent DMSO [19].

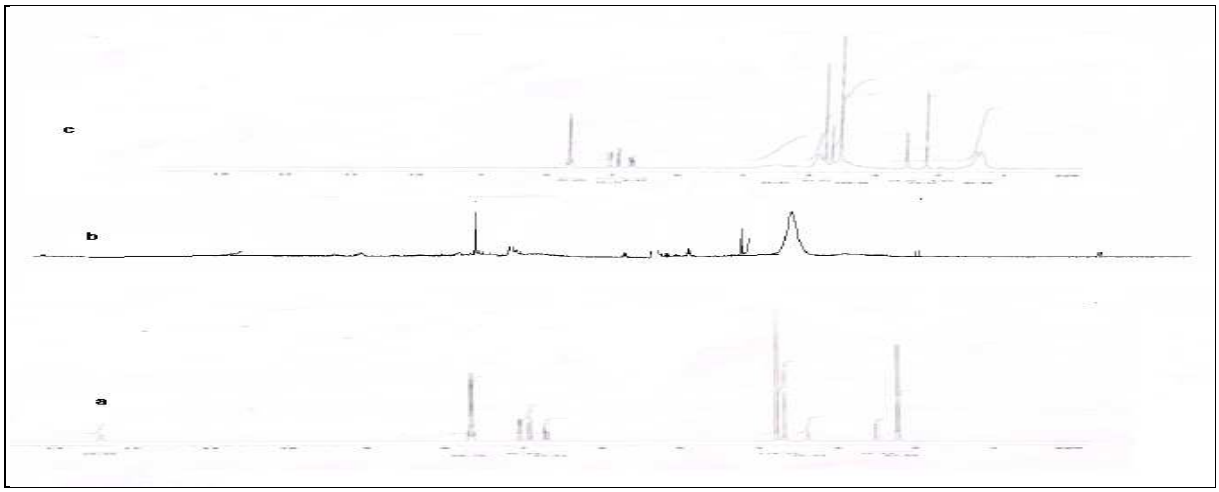

Fig.6: Overlay of comparative NMR spectra of pure drug, polymer, IND- Kollicoat IR

Solid dispersions prepared by solvent co grinding method (a)Pure IND, (b) Kollicoat IR (polymer), (c) Solvent drop co grinding method

4.8 Stability studies of solid dispersions:

Stability of amorphous IND in the solid dispersion is challenging problem. The stability issues of solid dispersions involve the aggregation of powder and crystal growth. Kollicoat IR served as an inhibitor of crystal growth by adsorbing to the surface of the IND particles, not only providing a barrier to aggregation but also shows good wet ability. After 6 month of storage samples were analyzed for drug content, dissolution study, FTIR and PXRD study. The dissolution performance and drug content were all similar to that at time 0. The results are shown in (Table 4)In order to study stability and possible solid state changes of developed solid dispersions after 6 months of storage FTIR and PXRD were carried out (fig 7, 8). The results after 6 month of storage there was no noticeable change in spectra of formulation additionally no other solid state transformations were detected. The comparative RDC of formulations at time 0 and 6 months shown in **(**Table 5**)** The results of stability study revealed that the IND Kollicoat IR solid dispersions prepared by various methods were physically and chemically stable for at least 6 months. Stability of solid dispersions due to high conformational entropy and low molecular mobility. Here Kollicoat IR is mainly responsible for stability of amorphous IND in solid dispersions, and mechanism proposed for stabilization is intermolecular hydrogen bonding between drug and polymer or polymer interacting specifically with functional groups of the drugs. It leads more miscibility of drug and polymer increases the Tg of miscible mixture thereby reducing the molecular mobility at regular storage temperature. The effect of moisture on the storage of stability of amorphous pharmaceuticals also significant concern because it increases molecular mobility and crystallization. Kollicoat IR has superior oxygen and moisture barrier properties. Amphiphilicity of kollicoat IR compared with the hydrophobic chains leading to adsorption on the surface of hydrophobic drugs and hydrophilic chain acts as stearic barrier so it impede aggregation and agglomeration and prefer stabilization[20].

TABLE 4: STABILITY STUDYOF SOLID DISPERSIONS

FC	%DC		%DR	
	0	3 mo	0	3 mo
F1	95.88±0.09	92.27±0.05	41.47±0.02	39.75±0.04
F2	97.20±0.02	95.07±0.01	80.86±0.01	76.84±0.019
F3	98.80±0.01	94.87±0.06	76.08±0.03	70.37±0.06
F4	98.74±0.02	94.67±0.04	56.25±0.05	55.97±0.002
F5	96.86±0.02	93.47±0.02	64.43±0.035	62.81±0.063

After 3 (mo) month of storage physical mixture and solid dispersions analyzed for %DC=drug content, %DR=drug release. All values are mean ± standard deviation of three determinations.

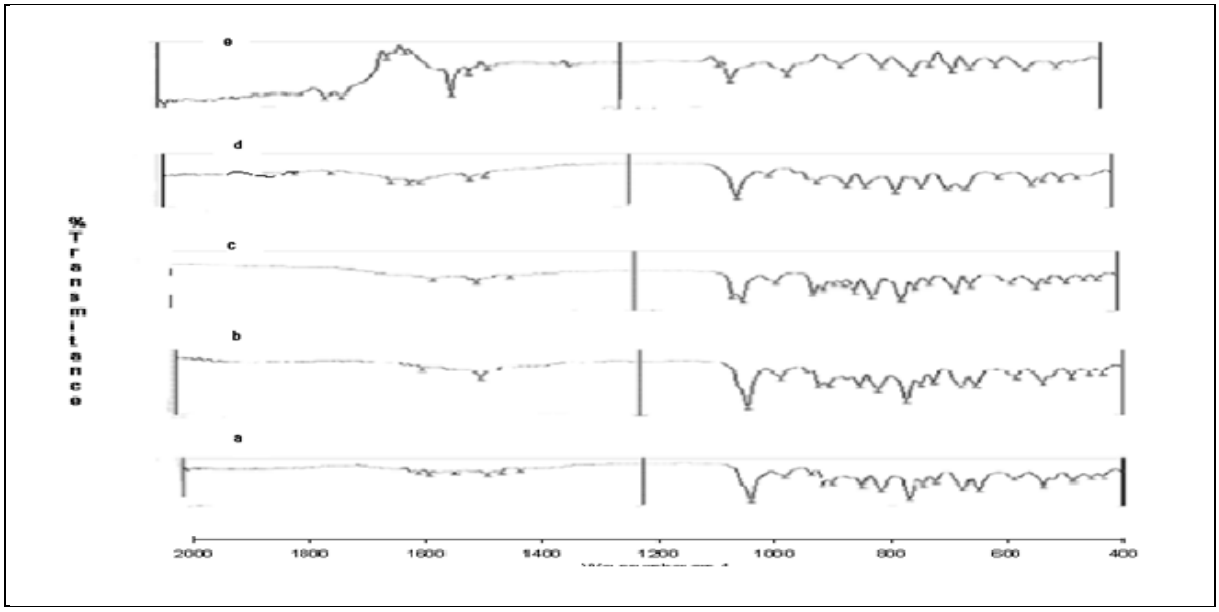

Fig.7: FTIR spectra of physical mixture and IND- Kollicoat IR solid dispersions after 3 month storage at room temperature.
(a) Physical mixture (b) Cogrinding, (c) Solvent drop cogrinding, (d) kneading. (e) Solvent evaporation.

TABLE 5: STABILITY STUDYOF SOLID DISPERSIONS BY PXRD

FC	Angle 2θ	RDC	
		0	3 mo
F1	11.62	0.94	0.95
F2	11.62	0.67	0.68
F3	11.62	0.62	0.61
F4	11.62	0.59	0.61
F5	11.62	0.47	0.49

After 3 (mo) month of storage RDC= relative degree of crystallinity of physical mixture and solid dispersions were calculated and compared.

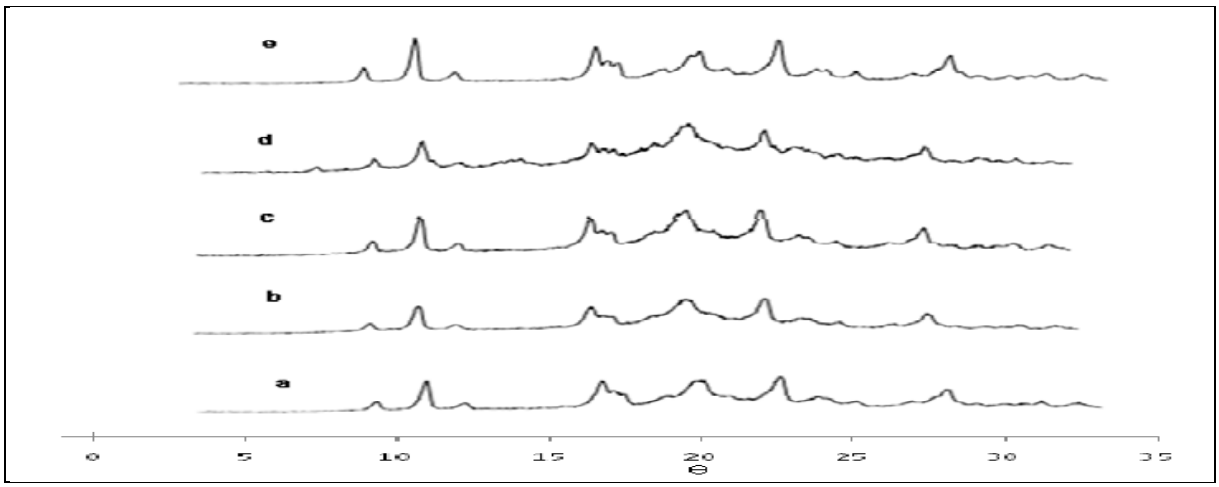

Fig.8: Overlay of comparative XRPD Diffractograms of physical mixture and IND- Kollicoat IR solid dispersions after 3 month of storage at room temperature.(a) Physical mixture (b) Co grinding, (c) Solvent drop co grinding, (d) Kneading,(e) Solvent evaporation

CONCLUSION

Binary solid dispersions of indomethacin with kollicoat IR were successfully developed by using various preparative methods. Significant improvement in solubility and dissolution rate of drug was observed in all solid dispersions due to alteration of surface properties of drug. IND was partially transformed from crystalline state to amorphous state which was confirmed by DSC, PXRD and NMR. The results of this study showed that Kollicoat IR is valuable excipients in the formulation of solid dispersions of Indomethacin. It plays an important role in stabilizing the

amorphous form of drug through molecular interactions with IND and by increasing glass transition temperature of resulting mixture. Taking these results into consideration, it is believed that the formation of solid dispersions enhance the solubility of IND, which could increase the formulation bioavailability.

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