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Solubility Enhancement of Meloxicam Prepared via Binary and Ternary Phases Using Spray Congealing

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ABSTRACT

In this work, the utilization of a spray congealing technique was adopted to prepare enhanced release, solvent-free microparticles of meloxicam (Mel). The binary and ternary phases prepared by spray congealing with Polyethylene glycol 3000 (PEG-3) and Gelucire 44/14 (Gel-44) in different drug-to-polymer ratios were considered. The prevalent particle size (mean diameter) was in the range of 75-85 µm and the microparticles had good encapsulation efficiency up to 99.0 %. The formulations were characterized by solubilizing efficiency, physical properties, drug content and dissolution behavior. In addition, the anti-inflammatory activity was determined. The ternary system of Mel-PEG-Gel (T1, T2 and T3) was compared with those of the corresponding binary system of Mel-PEG (B1) or Mel-Gel (B2). Scanning electron microscope analysis showed that it was possible to obtain spherically shaped and non-aggregated microparticles, with slightly drug crystals evident on the surfaces of drug-loaded microparticles. Differential scanning calorimetry and X–ray diffractometry were used to investigate the solid-state physical structure of the prepared microparticles. The results from X-ray diffraction and differential scanning calorimetry showed the absence of well-defined drug–polymer interactions. The solubility of binary phases (B1 or B2) was lower than the ternary phase's formulae (T1, T2 and T3). Consequently, the ternary phases as a carrier represents the most promising approach to the dissolution rate enhancement of meloxicam. From the in vitro release data, the selected formula prepared by spray congealing (T3) was enhanced the solubility and dissolution rate rather than other preparation techniques (physical mixture and solid dispersion by melting method). Finally, the microparticles prepared by spray congealing (T3) containing 10% Mel, 45% PEG-3 and 45% gelucire 14/44 exhibited higher anti-inflammatory activity on the paw edema of rats in comparison to the drug alone, physical mixture and solid dispersion.

INTRODUCTION

The enhancement of oral bioavailability of poorly water-soluble drugs remains one of the most challenging aspects of drug development. Several strategies have been developed to overcome this problem such as complexation, solubilization, and the formulation of solid dispersions. Meloxicam is a COX-2 inhibitor used to treat joint diseases such as osteoarthritis, rheumatoid arthritis and other musculoskeletal disorders. It is practically insoluble in water [1]. Solid dispersion is one of the most common techniques used to improve the dissolution of poorly soluble drugs [2]. It is defined as the dispersion of one or more active ingredients in an inert hydrophilic carrier or matrix in a solid state, prepared by the solvent evaporation [3], fusion [4], melt adsorption [5, 6], spray drying [7], spray freezing [8], melt extrusion [9], supercritical fluid precipitation [10], and spray congealing [11]. The advantages of using a spray congealing process are numerous. Generally, no solvent is required in the formulation and manufacturing process. Processing times are often shorter because solvent evaporation is not required. Undesirable drug–solvent interactions are eliminated [12]. Spray congealed microparticles are typically spherical with smooth surfaces; therefore good flow properties can be expected. This is advantageous when such a product is intended for filling into capsules or compressing into tablets [13]. Spray congealing was successfully used for preparing microparticles loaded with some other drugs such as clarithromycin [14], indomethacin [11], propafenone hydrochloride [15], felodipine [16, 17], fenbufen [18], tetracycline hydrochloride, and lidocaine hydrochloride [19]. Recently it was demonstrated that this technology also offers a promising approach for protein drug delivery systems such as insulin [20] and bovine serum albumin [21].

The most commonly carriers that can be used in the spray congealing process can be divided into two basic groups, hydrophobic and hydrophilic carriers. Hydrophobic carriers include beeswax, carnauba wax, cetearyl alcohol, cetyl palmitate,

fats (glyceryl behenate, glyceryl palmitostearate, glyceryl stearate, glyceryl palmitate, softisan-154, stearic acid, and stearic alcohol [22] These carriers should be used to control the release of short half-life drugs such as verapamil hydrochloride [23], theophylline [24], insulin [20], and bovine serum albumin [21]. Whereas Hydrophilic carriers which including polyoxylglycerides (gelucire), poloxamer 188 and 407 (pluronic F68/F127), polyethylene glycols (PEG), and esters of polyethylene glycol, used when enhancement of the dissolution rate of poorly water-soluble drugs is required, like in carbamazepine [25], diclofenac [26], praziquantel [27] and glimepiride [28]. The selected carriers employed in our preparation among those are the use of polyethylene glycol (PEG-3) and Gelucires (Gel-44). PEG polymers are widely used due to their low melting point, low toxicity, high viscosity, wide drug compatibility and hydrophilicity. Gelucires belong to a family of materials which are made up of glycerides and fatty acid esters of polyethylene glycols; the compounds from this group which has been studied extensively are Gelucire 50/13 and 44/14 [29]. Gelucire-44/14 is a hydrophilic carrier which is frequently used for this purpose, the suffixes 44 and 14 refer to its melting point and its HLB value respectively. Mostly the incorporation of drugs into hydrophilic carriers using spray congealing via binary phase, has frequently been reported to increase the dissolution rate of poorly soluble drugs [11].

The aim of the present study was to clarify the comparison between binary Mel-PEG (B1) or Mel-Gel (B2) and new ternary system (Mel-PEG-Gel) with different ratios T1, T2 and T3 prepared by spray congealing to improve the solubility and dissolution rate of meloxicam. The work was further extended to compare between other two different traditional methods (physical mixing and solid dispersion as melting method) with the selected formula prepared by spray congealing.

MATERIALS AND METHODS

Meloxicam was kindly supplied by Boehringer Ingelheim Pharmaceutical Inc. (Germany), Polyethylene glycol 3000 was provided by BASF (Ludwigshafen, Germany), and its melting point varies from 56 to 63 °C (The Merck Index – Eleventh edition, 1989). Gelucire 44/14 was provided by Gattefosse (St. Priest, France), and it has a nominal melting point of approximately 44 ^{0}C. All other materials used were of analytical or HPLC grade.

Preparation of the Mel microparticles

Preparation of binary and ternary systems by spray congealing

The microparticles were prepared by spray congealing using a Buchi Mini Spray Dryer B-290 (Buchi, Switzerland). The spray congealing apparatus was cooled by applying a flow of cooled air for approximately 10 min until the temperature at the connection of the spraying tower with the cyclone had reached at least -10 ^{0}C. The nozzle placed on top of the apparatus and the polymer was atomized within the desired temperature range controlled by the nozzle temperature (60-70 ^{0}C), applying an atomization pressure of 4 bar. Meloxicam was dispersed in the molten polymer systems with an ultraturrax (TP 18/10 equipped with a S 25 N 10 G dispersing tool; IKA Laboratory Technology, Staufen, Germany) for 2 min at 10,000 rpm in the reservoir container of the nozzle. Subsequently, Meloxicam-polymer desperation was atomized at 70 ^{0}C with 1.5 bar spraying pressure. The microparticles were collected in the production vessels. The obtained microparticles were stored in a desiccator until further use. The product yield was calculated as the mass of microparticles obtained in the production vessels in relation to the mass of the suspension introduced in the spraying nozzle.

Physical mixture

A physical mixture (PM) of the selected formula was obtained by blending the components in a glass mortar. Meloxicam and two different carriers was accurately weighed, mixed well in the mortar then passed through a sieve (250 μm). The physical mixture preparation was stored in desiccator under vacuum till next use.

Solid dispersion prepared by melting method

The melting process is technically the less difficult method of preparing dispersions provided the drug and carriers are miscible in the molten state. The process employs melting of the selected formula in metallic vessel heated in an oil bath at 70 °C. Immediately after melting, the sample was poured onto a metallic plate, which is kept in ice bath until dry. The dried mass was pulverized and sieved (250 μm). The prepared particles were stored in a desiccator until further use.

Evaluation of the drug content

An accurately weighed amount of each preparation was dissolved in a small volume of methanol and further diluted in Phosphate buffer saline (PBS) pH 7.4. The content of meloxicam was determined spectrophotometrically at 362 nm. The meloxicam content was calculated using the calibration curve. Each sample was analyzed in triplicate.

Solubility Studies

An excess amount of the samples was placed in contact with PBS pH 7.4. The samples were shaken for 24 hr at 37 °C in a horizontal shaker. The supernatant was filtered through a Millipore filter (pore size 0.22 μm). Half ml of the filtrate was immediately diluted and assayed spectrophotometrically at 362 nm. Results from solubility determinations are presented as mean values with standard deviations. Each sample was analyzed in triplicate.

Characterization of the Mel microparticles

Particle size determination

Particle size was determined by laser light diffraction. The equipment consisted of a Malvern Mastersizer 2000 (Malvern Instruments, Germany) including a Scirocco 2000 module for dry measurement purposes operating at 3.0 bar air pressure. For dispersion, it had been established that a sufficient dispersion of particles but no milling occurs at this level of air pressure with evaluation of data by Malvern software version 4.0 using the Fraunhofer approximation as the evaluation algorithm. Particle size of mean diameter between d(0.10), d(0.50) and d(0.90), are reported based on volume [30].

Scanning electron microscopy (SEM)

The formulated Mel microparticles morphologies were investigated by scanning electron microscopy (SEM). Samples were mounted on an aluminum stubs using conductive carbon tape (LeitTabs; Plannet GmbH, Germany) and coated with gold by sputtering three times for 20 seconds (SEM Autocoating unit E2500; Polaron equipment LTD, UK). The scanning electron microscope was operated at an acceleration voltage of 15 kV. The selected magnification was 1500 × since it was enough to appreciate the general morphology of the powder under study.

X-ray diffractometry

X-ray was investigated the meloxicam and Mel formulations as solid dispersion using a Bruker diffractometer (WI 1140, Japan) and Cu-ka radiation. The diffractograms were run at 2.5 °C min^{-1} and a chart speed of 2°/2 cm per 2q angle.

Differential scanning calorimetry (DSC)

DSC was performed on meloxicam and its spray congealing formulations using a Perkin Elmer DSC-7 differential scanning calorimeter (Perkin Elmer, USA) equipped with a liquid nitrogen sub ambient accessory (Perkin-Elmer). The instrument operated under nitrogen purge gas at a rate of 20 ml/min. Samples (3 mg) were sealed in alumina pans (TA instruments, Belgium) and heated at a scanning rate of 5 °C / min from -10 to 300 °C.

Dissolution tests

In vitro dissolution studies of Mel and Mel formulations (Binary and ternary phases) prepared by spray congealing were determined. In addition, the selected formula (T3) prepared by PM and SD was determined. USP paddle method by dispersed powder technique was used. Samples equivalent to 7.5 mg of Mel was added to 500 ml phosphate buffer saline pH 1.2 and 7.4 at 37±0.5 °C and stirred at 50 rpm. An aliquot of 5 ml was withdrawn at different time intervals with a sterile syringe filter (pore size 0.22 µm). The withdrawn volume was replenished immediately with the same volume of the pre warm (37 °C) dissolution medium in order to keep the total volume constant. Percent of meloxicam dissolved at various time intervals was calculated from the regression equation generated from the suitably constructed calibration curve. Each sample was prepared and analyzed in triplicate.

Anti-inflammatory activity of Meloxicam prepared by different techniques adopting Carrageenan-induced rat paw edema method.

The rats were divided into five groups of six animals. The first group was challenged with a subcutaneous injection of 0.1 ml of 1% w/v solution of carrageenan (10 mg of carrageenan were dissolved in 1 ml of 0.9% saline) into the plantar side of the left footpad of the rats to induce edema. In the other four groups, 30 min before the carrageenan injection, the animals were treated orally with pure meloxicam and different meloxicam formulations (7.5 %) at dose of 2 mg/kg [31]. The photos of feet from a lateral view were taken immediately after injection (0 h) and then after 4 h of carrageenan injection (as maximum edema formation reached its peak after 4 h of carrageenan injection) [32, 33]. Photos were taken using a digital camera; foot thickness was measured from the photos as described by Maruyama *et al.* [34]. The edema was calculated by the difference of thickness between 0 and 4 h. The control rat received 0.1 ml of saline solution. We used a non-treated right foot of the same animal as a reference. Data was then converted to percentage change of paw thickness using the following equation:

Percentage change of paw thickness = [100 × ($Thick_{post}$ – $Thick_{pre}$) / $Thick_{pre}$]

Where, $Thick_{post}$ and $Thick_{pre}$ are the paw thickness after and before carrageenan injection, respectively.

RESULTS AND DISCUSSION

Spray congealing is a rapid and simple process to prepare microparticles. The setting of different parameters, however, can affect the quality of the final product. In addition, the rapid solidification of the melting polymers from the droplets will influence the crystalline structures of spray congealing formulations [35].

Particle size distribution of Meloxicam-loaded microparticles

Particle size distributions of Mel with binary and ternary system prepared by spray congealing are shown in Table 1. The mean particles size diameter of Meloxicam formulations with B1, T1, T2, T3 and B2 were ranged from 75.4 to 85.3 µm. The selected formula of Mel-PEG-Gel (T3) prepared by PM, SD and SC had mean diameters of 175.0, 194.0 and 79.2 µm and span 2.8, 3.1 and 1.7 respectively. The span value gives an indication about the particle size distribution, when the value is not more than two; this is an indication for good particle size distribution (narrow distribution). From the results, the microparticles prepared by spray congealing were smaller with high particle distribution than the PM and SD particles. The yield values for spray congealing formulations were between 80.5 to 85.8 % for different batches.

Drug Content

The actual drug content of meloxicam in microparticles was

Table No.1: Formulation, yield, particle size distribution, drug content and solubility of Mel microparticles, prepared by spray congealing and Mel formulation by PM and SD.

Formula code	Mel [%]	PEG-3 [%]	Gel-44 [%]	Yield [%]	Mean diameter [µm]	span	Drug content [%]	Solubility [mg/ml]
Mel	-	-	-	-	-	-	-	0.212+2.4
B_1	10	90	-	80.5±1.7	85.3±1.5	2.0±2.0	93.4 ±2.8	1.287±3.6
T_1	10	80	10	83.6±1.8	80.5±3.1	1.9±1.5	97.5±3.6	1.346±2.5
T_2	10	65	25	84.3±2.0	82.9±3.5	1.8±1.8	98.2±3.1	1.442±3.4
T_3	10	45	45	85.8±1.7	79.2±2.4	1.7±1.6	99.0±2.5	1.685±3.6
B_2	10	-	90	83.5±2.5	75.4±3.6	1.9±1.9	94.3±2.6	1.217±3.6
T_3_PM	10	45	45	99.5±1.5	175±3.9	2.8±2.0	98.9±2.4	0.674±2.4
T_3_SD	10	45	45	98.3±1.9	194±4.4	3.1±1.7	99.5±3.4	1.409±3.4

Data of content evaluation were shown as the average ± S.D. (n=3).

found to be in the range of 93.4–99.5% of theoretical drug content (7.5 %, w/w) for microparticles prepared by spray congealing and different techniques (Table No.1). From the results, the drug content for ternary phase was higher than binary phase, in ternary phase the drug content increased with increasing the concentration of gelucire-44. This could be attributed to the hydrophilic and hydrophobic characters (HLB =14) of the gel-44.

Solubility Studies

The solubility studies indicated an increase in the solubility of meloxicam loaded microparticles prepared by spray congealing more than pure drug (Table No.1). The solubility values of ternary phases were 1.346, 1.442, and 1.685 mg/ml for T_1 T_2 and T_3 respectively. And with the binary phases was measured 1.287 and 1.217 mg/ml for B_1 & B_2 respectively. From the results, the solubility of the drug with ternary phase was larger than binary phases. Which could be probably be explained by increased the wettability of drug and micellar solubilization. Indeed, Gel-44 causes a decrease of the interfacial tension between the drug and the dissolving solution. In addition, the solubility of selected formula prepared by PM, SD and SC were 0.674, 1.409 and 1.685 mg/ml for T3_PM, T3_SD and T3_SC respectively. The solubility of microparticles prepared by spray congealing increased rather than other techniques (physical mixture and solid dispersion), which could be attributed to increase the wettability of drug via a decrease in the particle size, with increased the specific surface area when dissolved in aqueous solution.

Scanning Electron Microscope

The SEM pictures of Mel raw materials were characterized by irregular shaped crystals form Figure 1A. Whereas, PEG-3 and Gel-44 formed big polygonal particles with irregular shape and size (Figure 1B, C, in the left column) was showed. The physical mixture of T3_PM (Mel-PEG-Gel) particles contains the characteristic Mel crystals with adhering the polymer particles (Figure 1D). In case of SD, it was difficult to distinguish the presence of Mel crystals. Mel crystals appeared to be incorporate into the particles of the polymers (Figure 1E). In contrast, the spray congealing microparticles prepared from binary phase of Mel-PEG (B1) represented spherical particles with slightly rough surfaces (Figure 1F), while the microparticles prepared by spray congealing with gel-44 (B2) was showed as small homogenous and amorphous aggregates of spherical particles with smooth surfaces (Figure 1J). For ternary phase, the microparticles with regular spherical shape were obtained from all drug-to-carriers ratios. The surface smoothing of microparticles was improved with low crystallinity of drug appear on the surface with gradual increase in the concentration of Gel-44 as shown in Figure 1G, H and I for (T1, T2 and T3 at 10, 25 and 45% respectively). These observations provide the evidence of solid solution formation and are in accordance to the results obtained from DSC studies [36].

X-ray diffraction analysis

The powder X-ray diffraction patterns of various Mel, PEG-3, Gel-44 and its binary and ternary systems were compared in Figure 2. The diffraction pattern of the pure drug showed its crystalline nature, as indicated by the numerous distinctive peaks appeared in X-ray at diffraction angles of 2θ at 13.06, 14.92, 18.6, 19.22 and 25.8. The PEG-3 alone exhibited four high intensity peaks at 13, 19, 23 and 27^0. However, the Gel-44 exhibited two mean peaks with high intensity at 19.13 and 23.55. The decrease in the intensity of Mel peaks in the diffractograms of the binary phase microparticles (B1 and B2) and further decreasing with

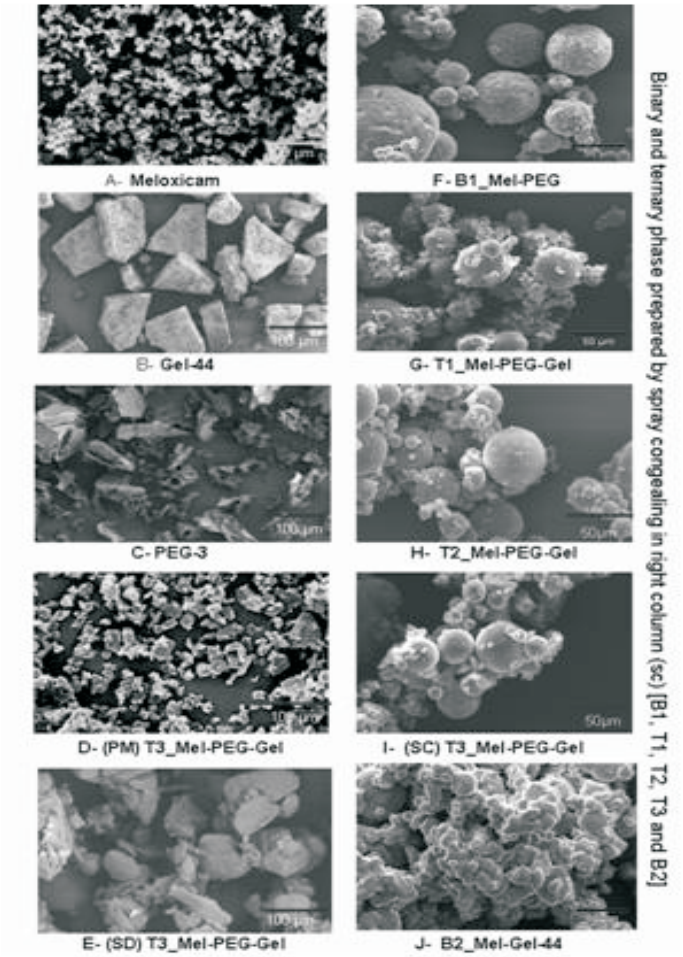

Fig. 1: SEM pictures of meloxicam systems: **A-** Mel, **B-** Gel-44 **C-** PEG-3 ,**D-** PM_Mel-PEG-Gel, **E-** T3_SD and binary and ternary phases prepared by spray congealing in right column (**F-** B1, **G-** T1, **H-** T2, **I-** T3-SC and **J-** B2).

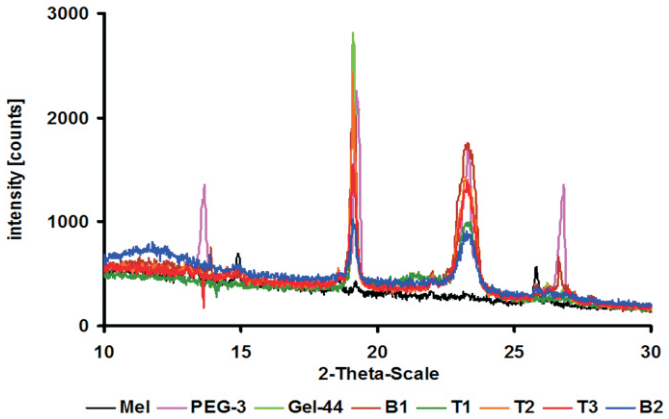

Fig. 2: X-ray diffractograms of meloxicam, PEG, Gel and meloxicam formulation prepared by spray congealing with binary phase (B1, B2) and ternary phase (T1, T2 and T3).

decreasing Mel-content until complete disappearance in ternary phase (T1, T2 and T3) prepared by spray congealing were observed. Thus, the spray congealing process decreased the crystallinity or the disordered molecular dispersion of the crystalline drug in the binary and ternary phase microparticles during rapid cooling of the sprayed droplet. No new peaks could be observed suggesting the absence of any chemical interaction

DSC Studies

Figure 3, demonstrated thermograms of Mel, PEG-3, Gel-44 and their binary and ternary phase prepared by spray congealing (SC). The DSC thermograms of each component exhibited a sharp endothermal peak corresponding to the melting point of Mel, PEG-3 and Gel-44 (257.38, 61.58 and 46.56°C respectively). The thermograms of the binary phase containing an excess amount of Mel demonstrated one endothermic transition close to the melting temperature of PEG-3 or Gel-44 as mention above. In case of ternary phase, the thermograms containing an excess amount of Mel demonstrated two endothermic transitions. The first transition peak was observed to the melting temperature of the Gel-44 which gradually shifted to the lower temperature, losing its sharp and distinctive appearance. Whereas, the second minor transition peak was observed very close to the melting temperature of PEG-3. The disappearance of the drug melting in lower amount of Mel (7.5 %) was due to it is completely dissolution in the melted carriers (in binary and ternary systems). When compared between the PM, SD and SC, there is no differences were apparent of DSC thermograms data (Figure 4). The complete disappearance of the drug-melting peak observed in different formulations process (PM, SD and SC) was attributed to the drug dissolution in the melted carrier before reaching its fusion temperature [38]**.** The results of DSC and X-ray indicated the disappearance in crystallinity of Mel in presence of higher amount of PEG-3 and Gel-44.

In vitro dissolution

The in vitro release study of Meloxicam and Mel-formulations prepared by spray congealing were carried out in 0.1 N HCl (Fig. 5a) and phosphate buffer pH 7.4 (Figure 5b). Generally, the release of Mel in phosphate buffer pH 7.4 was higher than in 0.1 N HCl. These results based on the limited solubility of meloxicam in acidic medium [39]. The in vitro dissolution characteristics of different types of preparations were compared with the pure drug. From Figure 5b, the microparticles prepared by spray congealing with ternary phase of Mel incorporate in PEG with different ratios of Gel-44 was showed improve dissolution when compared with those prepared via binary phase (B1 or B2). In ternary phases, the dissolution profile of microparticles with three different ratios (10, 25 and 45% of Gel-44 to PEG-3) was affected by gelucire concentrations. As the proportion of Gel-44 in the microparticles increased, the dissolution rate was increased. The ability of Gel-44 as surfactant to accelerate the in-vitro dissolution of poorly water soluble drugs has been attributed to wetting, micellar solubilization, and / or deflocculating effect of surfactant. Since, one of the techniques that have been synergistic effect in dissolution of insoluble drugs is the incorporation of gelucire with hydrophilic carrier (PEG). From the results, T3 which showed the highest dissolution rate was selected to be prepared by other different techniques (PM and SD). The maximum dissolution rate of meloxicam was observed for the microparticles prepared by spray congealing rather than the solid dispersion and physical mixture (Figure 6). This could be attributed to the fact that microparticles prepared by spray congealing result in more uniform drug dispersion with particle size reduction and less aggregate as compared to those prepared by the PM and SD methods. The mechanisms responsible for the improved dissolution rate of a drug in the spray congealing microparticles can be contributed by several factors; besides to the improved wetting and solubilization of Mel by the hydrophilic carrier evidenced by the solubility measurements. The reduction of the drug particle size and the transformation of the solid state of

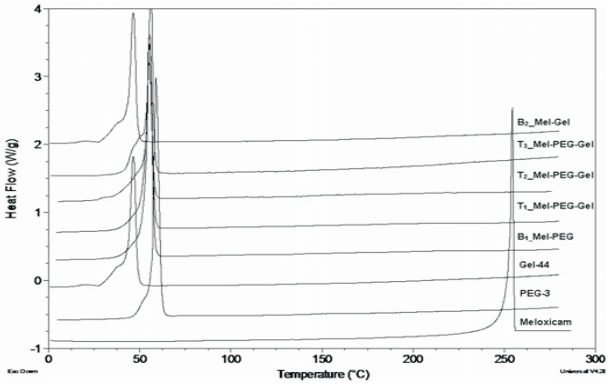

Fig. 3: DSC Thermograms of meloxicam, PEG, Gel and meloxicam formulation prepared by spray congealing with binary phase (B1, B2) and ternary phase (T1, T2 and T3).

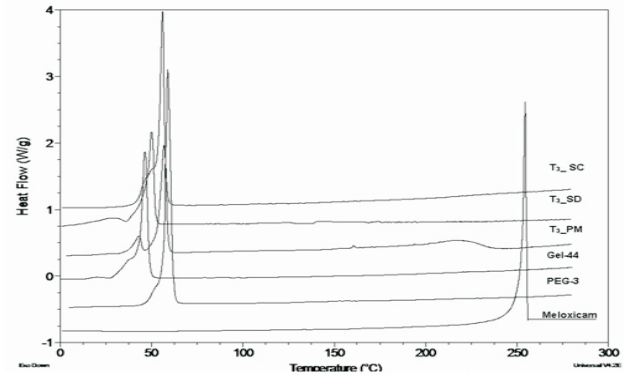

Fig. 4: DSC Thermograms of meloxicam, PEG, Gel and meloxicam selected formula prepared by physical mixture (T3_PM), solid dispersion (T3_SD) and spray congealing (T3_SC).

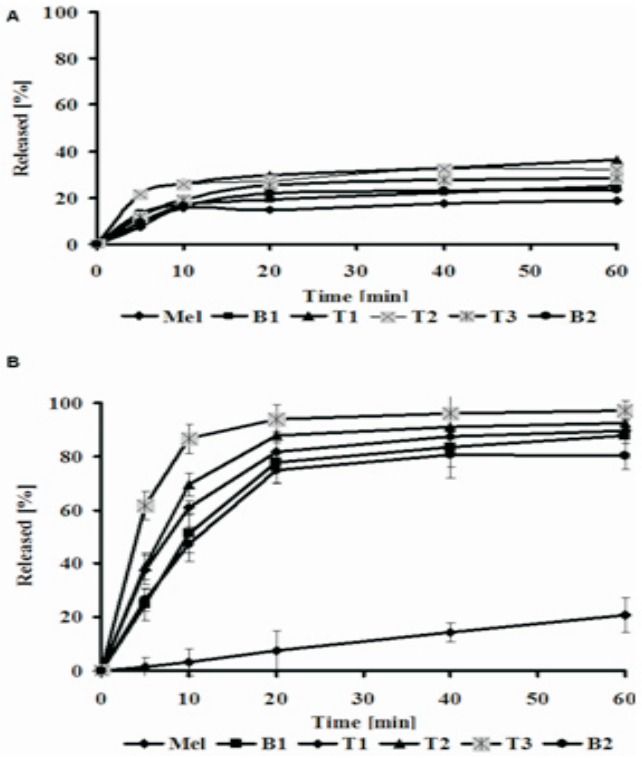

Fig. 5: (A) Release profiles of meloxicam and mel formulation prepared by spray congealing with binary phase (B1, B2) and ternary phases (T1, T2 and T3) in 0.1 N HCl pH 1.2. **(B)** with phosphate buffer saline pH 7.4.

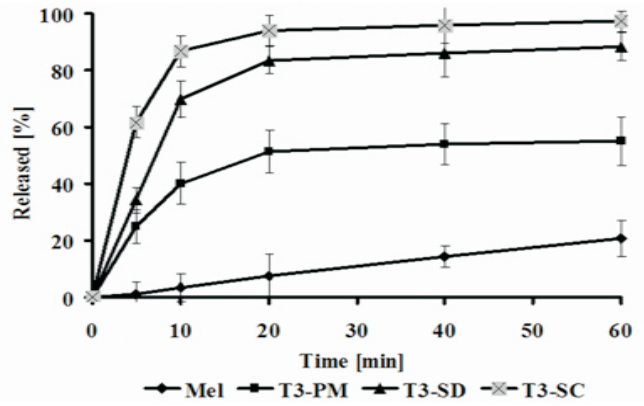

Fig. 6: Release profiles of meloxicam, and meloxicam selected formula prepared by physical mixture (T3_PM), solid dispersion (T3_SD) and spray congealing (T3_SC).

the drug from a crystalline form into the amorphous state or from a polymorphic form to a different one could be involved for solubility enhancement [40]. The improvement of dissolution rate of different Mel-formulations was confirmed by the previous data of DSC and X-ray analysis.

Anti-inflammatory activity of Meloxicam prepared by different techniques adopting on Carrageenan-induced rat paw edema thickness method

Oral administration of 2 mg/kg Meloxicam bulk powder (Bulk meloxicam) or different formulae prepared by physical mixture, solid dispersion and spray congealing (T3_PM, T3_SD and T3_SC) 30 min before carrageenan-induced rat paw edema; to allow its absorption significantly reduced its thickness [32]. Figure 7A, illustrates the anti-inflammatory activity of microparticles prepared by different techniques, (SC, SD and PM) and drug alone on the hind paw of the rats. Data comparisons were performed using one-way ANOVA followed by Dunnett's test. All of the prepared microparticles inhibited significantly ($p < 0.001$) the percentage thickness of edema, as compared with control group, and this action persisted for four hrs after carrageenin injection. Photos shows edema rat paw thickness method after carrageenan injection and the suppression effects of meloxicam and Mel-formulations on edema thickness (Figure 7B). The result showed that the edema inhibition by meloxicam and meloxicam formulations (SC, SD and PM) could be arranged in a descending order as T3_SC > T3_SD > T3_PM > Mel > control.

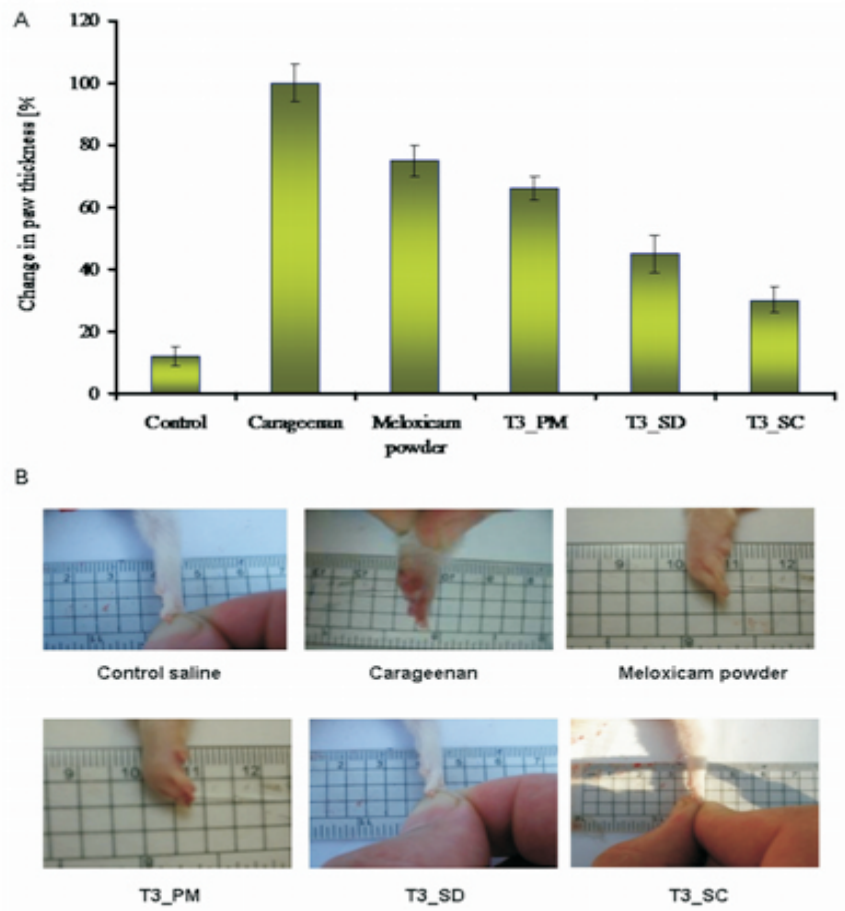

Fig. 7: (A) Anti-inflammatory effect of meloxicam and different meloxicam formulations using Rat-Pow edema method. **(B)** Photos shown edema rat paw thickness after carrageenan injection and the suppression effects of meloxicam and Mel-formulations on edema thickness

CONCLUSION

The present work demonstrated the preparation of solid dispersions of meloxicam with polyethylene glycol 3000 and Gelucire 44/14 with different drug-polymer ratios prepared by spray congealing method, with the improved solubility and dissolution properties of meloxicam. Spray congealing was successfully used for preparing microparticles loaded drug with relatively high total process yields up to 85.8% and drug content up to 99.0%. SEM showed that the product consists mainly of

primary microparticles of ideal spherical shape and smooth surfaces with various hydrophilic carrier materials, and demonstrated the difference between binary and ternary phase. The DSC and X-ray studies clarified the physical state of both the drug and the carriers in the samples, No new peaks could be observed suggesting the absence of any chemical interaction between meloxicam and the matrix. The selected formula prepared by spray congealing (T3) was enhanced the solubility, dissolution rate rather than other preparation techniques (physical mixture and solid dispersion by melting method). Moreover, T3_SC had superior anti-inflammatory activity than the drug itself, T3_PM and T3_SD. Spray congealing is a promising manufacturing method to be employed and developed for industrial-scale microparticles preparation. It is expected to gain wide spread use due to the recent growing interest in melt technologies, especially for taste masking, controlled release, and solubility enhancement

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