Original Article

Preparation and Characterization of Directly Compressible Spherical Agglomerates of Etoricoxib

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ABSTRACT

Aim: The current work contemplates formulation of spherical agglomerates of Etoricoxib, with a view to improve the flow properties, solubility and dissolution rate. **Materials and Methods:** Spherical agglomerates of etoricoxib were produced employing quasi emulsion solvent diffusion method using hydrophilic polymers like PVP K30 and PEG 6000. IR spectroscopy and Scanning Electron Microscopy along with physicochemical evaluations were used to characterize the agglomerates. **Results:** The optical microscopic studies indicated that the agglomerates were spherical in shape and varied in size from 1203.9 ± 126μm to 1297.2 ±164.2μm. The technique was found to enhance the aqueous solubility of the drug from 1.45 μg/ml to 8.26±0.05 μg/ml and the dissolution in 60 min from 39.57% to 82.88%. Etoricoxib tablets prepared using spherical agglomerates with PVP K30 and PEG 6000 displayed dissolution of 82.88% and 76.89% respectively that were considerably higher than conventional etoricoxib tablets. **Conclusion:** From the dissolution profile and % cumulative release from formulations it was concluded that Spherical Agglomeration technique substantially improves the flow properties, aqueous solubility and rate of dissolution of etoricoxib.

Key words: Etoricoxib, Spherical, Agglomerates, Directly compressible, Flow properties, Rate of dissolution.

INTRODUCTION

Direct compression is a simple and economical technique for tableting which has fewer steps and suited for drugs prone to be affected by heat or moisture.[1] However, owing to deficient binding or bonding properties, many drugs are not able to be directly compressed.[2] Hence, it becomes necessary to include large amounts of directly compressible excipients that invariably increase the production cost. To overcome this limitation, an attractive avenue is modification of physicochemical properties of the drug by different particle engineering strategies.[3] One such technique gaining popularity is Spherical Agglomeration (SA) that employs comparatively fewer steps in tableting process. SA involves simultaneous crystallization and agglomeration to obtain a compact spherical material that leads to improved flow ability as well as compressibility and thereby proves cost effective.[4]

Spherical crystallization technique necessitates the use of three solvent systems in the form of a dispersion medium, solvent for dissolution of the substance and the wetting or bridging solvent.[5] The technique produces spherical agglomerates (SAs) that can be employed as intact spheres or directly compressible material with adequate micrometric, compressional and dissolution properties. Spherical agglomeration may be used as a technique for particle size enlargement by adding an immiscible bridging liquid to agglomerate crystals prior to deliquoring.[6] Addition of bridging liquid to drug solutions results in

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immediate agglomeration. Improved flow ability and compressibility can be achieved by adjusting the amount of bridging liquid and the stirring speed.[7,8] The SAs can be used as final dosage form in capsules. It is possible to change the proportion of excipients used in the SA to obtain predictable drug release. The SAs having different drug release properties can be color coded too. It is possible to formulate the SAs of only excipients, which can be used as placebo therapy.

Etoricoxib (ETX) is a NSAID belonging to second generation cyclooxygenase-2 (COX-2) inhibitor that is prescribed as an analgesic and anti-inflammatory drug for arthritic ailments like rheumatoid arthritis. A number of specialized formulations of etoricixib for injectable and transdermal administration have been developed for treatment and management of musculoskeletal disorders. Bio-adhesive hybridized polylactic acid-based nanoparticles of the drug have been proposed for intra-arterial administration in the treatment of osteoarthritis.[9] Poly (caprolactone) micro particles loaded composite chitosan gel has been developed for intrarticular depot delivery for treatment of osteoarthritic condition.[10] An ethosomal formulation of the drug is proposed for management of skin inflammation.[11] However, peroral route continues to be the most preferred mode of administration for etoricoxib. But, the major problem associated with the drug is its poor aqueous solubility resulting in low dissolution rate. The drug is also known to possess poor micrometric property as well. Considering these drawbacks, the present study aimed to produce SAs of etoricoxib to enhance solubility, micrometrics and rate of dissolution.

MATERIALS AND METHODS

Etoricoxib was a gift sample from Indian Fine Chemicals Private Limited, Mumbai, India. PVP K30 polymer was procured from Colorcon Private Limited, Verna, Goa, India. All other chemicals and solvents of analytical grade were procured from Sd Fine Chemicals, Mumbai, India.

Preformulation and solubility studies

Flow properties of etoricoxib was determined by measuring the angle of repose by fixed funnel method. Properties like Bulk density, Tapped density, Hausner's ratio, Carr's index were also measured.[12]

Solubility studies of etoricoxib were done according to method described by *Higuchi and Connors*. An excess quantity of drug was taken in vials containing 10 ml of media. The vials were shaken in water bath (100 strokes per min) for 24 hr at room temperature. The solutions were then filtered using Whatman filter paper and the solubility of the drugs were analyzed spectrophotometric ally after suitable dilutions. The solubility of the drug was determined in distilled water, pH 1.2 buffer solution.

Drug-Excipients interaction

Infrared (FTIR) spectroscopy

FTIR scanning was employed to detect presence of any chemical interaction of the drug with formulation excipients. The powdered sample and dry powdered potassium bromide were mixed thoroughly. The resulting mixture was loaded in a diffuse reflectance sampler and scanned over the wavelength range of 4000-400 cm^{-1} in an FTIR spectrophotometer (Jasco 460 plus, Japan). The IR spectrum of the physical mixture and SAs were compared with the spectra of ETX to detect any possible interaction between ETX and excipients used.

Preparation of agglomerates by Quasi Emulsion Solvent Diffusion (QESD) Method

A solution of ETX (1g) was prepared in ethanol (5ml) used as a good solvent. About 1ml of chloroform was added as a bridging solvent to the solution of drug in ethanol to obtain a clear solution, which was then added drop wise into aqueous solution (75ml) of polymer.[13] The type and amount of polymer in the aqueous phase was varied as indicated in Table 1. The mixture produced was stirred at 1000 rpm at constant rate for 30 min. The resulting SAs were then recovered by filtration and subjected to drying at room temperature.

Characterization and evaluation of agglomerates

Scanning Electron Microscopy (SEM)

SEM was employed to examine the surface topography and morphology of prepared SAs.[14] To enhance the conductivity, an ion sputtering device (JEOL, JFC-1100 E, Japan) was used for 5 min under reduced pressure (0.001 torr) to coat gold (200ºA) on the samples, which were then subjected to SEM (JEOL, JSM-840A, Japan).

Estimation of drug content

Powdered SAs containing 50 mg ETX was weighed and solubilized in buffer (pH 1.2). Subsequently, the solutions were filtered (0.45µm, Millipore) and suitably diluted to

Table 1: Formulation composition of various batches of agglomerates.

Agglomerate Ingredients	SA1	SA2	SA3	SA4	SA5	SA6
Etoricoxib (g)	1	1	1	1	1	1
PVP K30 (g)	1	2	3	-	-	-
PEG 6000 (g)	-	-	-	1	2	3

determine the drug content with UV spectrophotometer at 233 nm (Jasco UV spectrophotometer) using buffer (pH 1.2) as blank. From the absorbance, drug content of the SAs was calculated using equation 1.

$$\text{Drug content (\%)} = \frac{\text{Calculated amount of drug in agglomerates}}{\text{Theoretical amount of drug in agglomerates}} \times 100 \quad \text{-------(1)}$$

Determination of Micromeritic Properties

Determination of Tapped Density was undertaken by transferring SAs (20g) into a 50 ml measuring cylinder. Using a bulk density apparatus (M/s Cambell Electronics, India), the cylinder was tapped to a constant volume at 100 strokes/min.[12] Likewise, bulk density was found out by loading same amount of granules into the measuring cylinder and tapping it three times in the same apparatus at the same speed. The final volumes were noted down in each case and using equations 2 and 3, the tapped density and bulk density were calculated respectively. The Carr Compressibility Index and Hausner ratio of SAs was computed from the values of the tapped density and bulk density using equations 4 and 5 respectively.

$$\text{Tapped density} = \frac{\text{mass (g)}}{\text{tapped volume (ml)}} \quad \text{------(2)}$$

$$\text{Bulk density} = \frac{\text{mass (g)}}{\text{Bulk volume (ml)}} \quad \text{-----(3)}$$

$$\text{Compressibility Index (\%)} = \frac{\text{Tapped density} - \text{Bulk density (g)}}{\text{Tapped density}} \times 100 \quad \text{-----(4)}$$

$$\text{Hausner's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}} \quad \text{------(5)}$$

Determination of angle of repose

Fixed funnel method was adopted, wherein at a constant height of 2.5 cm above a horizontal surface, a funnel was secured through which the SAs were carefully allowed to pass until the tipof the cone-shaped assemblage just came in contact with the lower funnel tip.[12] Measuring the height and diameter of the assemblage enabled the calculation ofthe angle of repose using equation 6.

$$\theta = tan^{-1}\frac{H}{r} \quad \text{-------(6)}$$

Where *r* and *H* represent the radius and height of the cone-shaped assemblage.

Determination of mean particle size

Optical microscopy was employed to determine the particle size of the prepared SAs.[15] The mean projected diameter of 400 SAs from each batch was measured with an eye piece micrometer that was calibrated with a stage micrometer at suitable magnification before the measurement of particle size.

Solubility Studies

Solubility studies of ETXand SAs were conducted as per method described by *Higuchi and Connors*. Drug in excess was taken in vials having 10 ml of distilled water. The vials shook on a water bath (100 strokes per min) at room temperature for a period of 24 hr. The resulting dispersions were subsequently filtered using Whatmann filter paper and the solubility of the drugs was analyzed spectrophotometrically after suitable dilutions.[16,17]

Preparation of the tablets by direct compression

The SAs were made to pass through a sieve to crush the lumps and 1 % w/w each of talc and magnesium stearate was added for lubrication (Table 2). The resultant SAs were subjected to compressioninto tablets using an 8.5 mm flat punch in a rotary 10 station compression machine. (RIMEK MINIPRESS) using a 'B' tooling to a hardness of about 5-6 kg/cm^2.

Table 2: Composition of tablet formulations.

Formulation	F1	F2	F3	F4	F5	F6
Agglomerates*	120mg	180mg	240mg	120mg	180mg	240mg
Talc	1%	1%	1%	1%	1%	1%
Magnesium Stearate	1%	1%	1%	1%	1%	1%

*The Tablets F1, F2, F3, F4, F5 and F6 contained agglomerates SA_1, SA_2, SA_3, SA_4, SA_5 and SA_6 respectively.

Evaluation of tablets

Thickness

The thickness of each of ten tablets randomly selected was measured by digital Vernier caliper. Digital caliper (Mitutoyo Corporation, Kawasaki, Japan) was used to record the values in mm. The mean and standard deviation of the thickness were calculated.[18]

Hardness

In order to determine the hardness using a Stokes Monsato hardness tester (M/s Cambell Electronics, India), from each batch of tablets, ten tablets were randomly selected. The hardness of each tablet was measured and expressed as kg/cm^2. The arithmetical mean and standard deviation were computed.[18]

Friability

A USP friabilator was used to determine the friability of tablets of each batch. About twentyweighed tablets from each batch were placed inside the friabilator that was operated for 4 min at 25 rpm.[18] Then the weight of the tablets was again determined. Equation 7 was used to calculate the friability.

$$Friability\,(\%) = \frac{\left(Initial\ weight - Final\ weight\right)100}{Initial\ weight} \qquad \text{----------(7)}$$

Weight variation test

The weight variation was determined as per the procedure prescribed in Indian pharmacopeia (IP). From each batch, 20 tablets selected randomly were individually weighed to compute the average weight and its standard deviation. If the deviation of the weights of 2 or less than two individual tablets from the average weight exceeds the permissible limit and none deviate by more than twice the limit then the batch is assumed to have passed the test. The maximum permissible limit is 7.5% for tablets weighing between 130 to 324 mg.[18]

In vitro disintegration time

As specified in IP, disintegration test apparatus was used to determine the disintegration time of all formulations. Six tablets were separately placed in each tube of disintegration test apparatus and the discs positioned. The temperature of water was controlled at 37 ±2°C and the time taken for the tablet to disintegrate completely was recorded.[19]

In vitro dissolution study

Each batch of tablets was subjected to dissolution study in a USP paddle apparatus. About 900 ml of HCl (pH1.2) used as the media was maintained at 37 ± 0.5°C and a paddle stirring speed of 50 rpm. Samplesmeasuring 5ml was withdrawn at a 10, 20, 30, 40, 50 and 60 min. and replaced every time with 5ml of the fresh buffer maintained at 37 ± 0.5°C. A spectrophotometer at 233 nm wavelength was used to measure the absorbance of the withdrawn samples to determine the drug release.[20] The cumulative drug released was plotted on Y axis versus time on X axis to obtain the dissolution profiles.

Statistical Analysis

The raw data generated were statistically compared by performing ANOVA in GraphPad 5.0 Instat demo version software (GraphPad Inc. CA, USA). The probability value of less than 0.05 was considered to be significant.

RESULTS AND DISCUSSION

Preformulation and solubility studies

When subjected to preformulation studies, ETX displayed a Hausner's ratio of 1.50 and Carr's index of 33.6% with an angle of repose of 30°. From these values it can be inferred that the drug has very poor flow properties. Poor flow properties can pose a problem in direct compression.[12] Solubility studies of ETX revealed an aqueous solubility of 1.45±0.07µg/ml, whereas solubility in pH 1.2 HCl buffer was 18.5±0.11µg/ml. This indicated that the drug has low solubility in water but is more easily soluble in pH 1.2 HCl buffer.

Infrared (FTIR) spectroscopy

The FTIR spectrum study revealed three prominent peaks at 2862.81 cm^{-1}, 3462.56 cm^{-1} and 1429.96 cm^{-1} which may be assigned to C-H stretch present in aliphatic group (Alkane), N-H group and C-C stretch respectively.

These prominent peaks of the ETX were also apparent in spectrum of the physical mixture at 2860.51 cm^{-1}, 3460.26cm^{-1} and 1425.76 cm^{-1}. Likewise, the characteristic peaks of ETX were observed at 2858.21 cm^{-1}, 3450.12 cm^{-1} and 1424.46 cm^{-1} in the spectra of the formulations. The appearance of drug characteristic peaks in the spectra of physical mixture as well as formulation indicates ETX had maintained its chemical integrity in the physical mixture and in the formulation. The studies thus rule out possibility of any drug-excipient interactions and therefore the potential incompatibility of the drug with other excipients used. IR has been used as a useful tool to study the possible incompatibility issues between drug and various excipients.[13]

Preparation of agglomerates by Quasi Emulsion Solvent Diffusion (QESD) Method

In the preparation of SAs of ETX, it was noted that the solvent system greatly influences the process of formation of SAs and their properties. Hence an important step in the formation of SAs was the selection of suitable solvent system. In the initial trials chloroform, dichloromethane, methanol, acetone-ethanol was used to prepare SAs, which performed the dual role of good solvent and bridging liquid. However, the SAs formed were irregularly shaped and some formulations appeared as opaque solutions. Hence in further trials, the above solvents were replaced with ethanol which proved a good solvent and chloroform which played the role of bridging liquid. With this solvent system, the SAs formed were discrete, free flowing and spherical with good micrometric properties.

After selecting a suitable solvent system, the next step was to optimize the process parameters. The SAs were prepared using different processing temperatures ranging from 5°C to 25°C. At 5°C, sticky fragments were formed. On the other hand, very few SAs with irregular shape and size were formed when the preparation was executed at 15°C. At room temperature (25 ± 5°C) SAs were formed with good yield, shape and size. Effect of agitation speed on the properties of SAs was also studied. The SAs were prepared at different rpms and stirring time to study the effect of agitation on their properties. At lower rpm (< 800) the SAs formed were not homogenous in size and irregular in shape while at higher rpm (> 1200 rpm), the SAs formed were very fine in size drastically hampering the flow properties. However, at 1000 rpm, the SAs formed were free flowing with good sphericity and flow properties. The time of stirring was also found to be critical in preparation of SAs. At stirring time of 5 min SAs were not formed whereas at 15 min, the SAs were partially formed. On the other hand, when the stirring was carried out for 30 min, the SAs were found to be completely formed. Based on these observations, a temperature of 25±5°C and stirring for 30 min at 1000 rpm was considered to be ideal for formation of SAs of ETX. Among the various hydrophilic polymers investigated, PVP K30 and PEG6000 were found most suitable to prepare SAs of ETX. PVP K30 was used in formulations F1 to F3 and PEG6000 in formulations F4 to F6 in varying concentrations.

Characterization and Evaluation of agglomerates

Scanning Electron Microscopy (SEM)

Scanning electron microscopic studies revealed that the SAs appeared to be discrete and near-spherical in shape. The optical microscopic studies indicated that the SAs of different batches were spherical in shape and varied in size from 1203.9 ± 126μm to 1297.2 ± 164.2μm (Figure 1).

Determination of micromeritic properties

SAs of ETX prepared with PVP K30 and PEG 6000 were found to significantly improve ($P < 0.05$) the flow properties. The angle of repose values of the SAs ranged from 21.1 to 22.7° while the Carr's index varied from 11.86 to 13.63% indicating a considerable enhancement in the flow properties. Likewise, the Hausner's ratio varied from 1.13 to 1.15 suggesting the 'good' flow properties of the SAs produced (Table 3). A Carr's index of 11-15 %, Hausner's ratio of 1.12-1.18 and angle of repose values of 20-30°suggests good flow properties.[15]

Solubility studies

ETX was found to exhibit poor aqueous solubility of 1.45 μg/ml on equilibrating with water for 24h. However, the technique of SA was found to significantly increase ($P < 0.05$) the solubility of ETX. The solubility

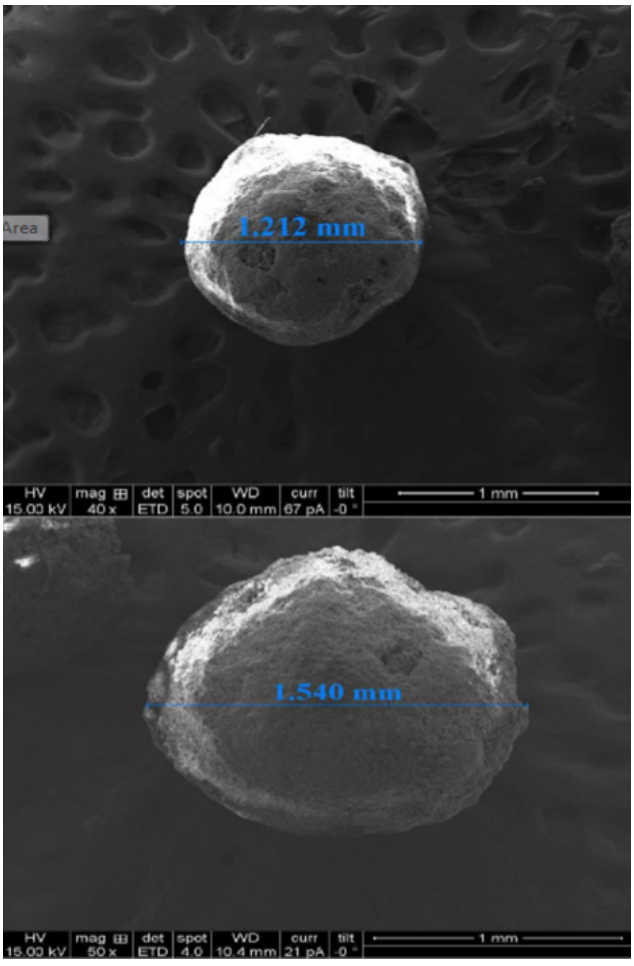

Figure 1: SEM of Spherical agglomerates of Etoricoxib.

Table 3: Micromeritic properties of etoricoxib and its spherical agglomerates.

Formulations	Bulk density* (gm/ml)	Tapped density* (gm/ml)	Carr's index (%)	Hausner's ratio	Angle of Repose	Solubility in water* (µg/ml)
Etoricoxib	0.83±0.02	1.25±0.06	33.6	1.50	30°	1.45±0.07
F1	0.44±0.04	0.50±0.07	13.63	1.13	21.5°	3.73±0.10
F2	0.58±0.03	0.67±0.01	12.51	1.14	22.1°	6.49±0.03
F3	0.60±0.04	0.69±0.03	13.04	1.15	22.7°	8.26±0.05
F4	0.41±0.10	0.47±0.06	12.76	1.14	21.1°	2.60±0.06
F5	0.48±0.02	0.55±0.01	12.72	1.14	21.8°	4.83±0.07
F6	0.52±0.06	0.59±0.05	11.86	1.13	22.4°	7.39±0.11

** The values represent mean ± SD*

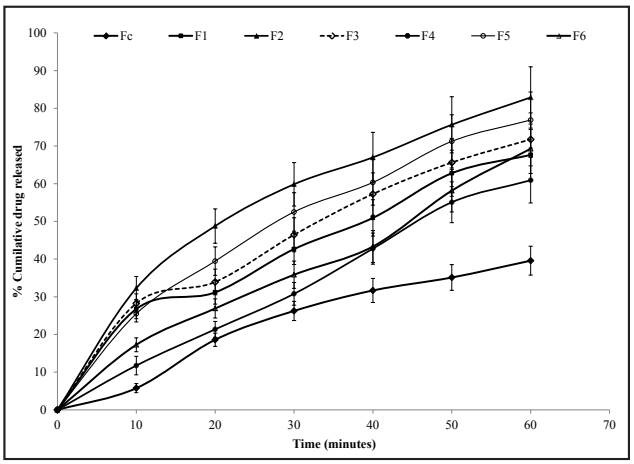

Figure 2: Dissolution profile of Etoricoxib tablets containing agglomerates prepared using PVPK30 and PEG6000.

of SAs were found to be 3.73±0.10, 6.49±0.03, 8.26±0.05, 2.60±0.06, 7.39±0.11, 4.83±0.07 µg/ml for SAs of batches F1, F2, F3, F4, F5 and F6 respectively. The increase in solubility of SAs can be ascribed to the hydrophilicity of the polymers. The enhancement of solubility in presence of PVP K30 can be attributed to its anti-nucleating property.

Further increase in the proportion of polymers failed to further increase the solubility of ETX.

Preparation and evaluation of tablets

SAs were further compressed into tablets after blending with talc (1%w/w) as a lubricant and magnesium stearate (1%) as a glidant. The resulting tablets were subjected to evaluation of tablet properties including hardness, thickness, weight variation, friability, disintegration time and *in vitro* dissolution of drug. The batches of tablets produced were found to conform to the Indian Pharmacopoeial specifications. The percentage cumulative release of drug from formulations F1, F2, F3, F4, F5 and F6 at 60 min was found to be 67.64%, 82.88%, 71.75%, 60.90%, 76.89% and 69.27% respectively (Figure 2). Formulation F2 was found to exhibit the highest cumulative release and therefore considered the ideal formulation. The likely reason for the better performance of the formulation can be attributed to the dispersing and anti-nucleating property of PVPK30. The other formulation that gave a comparable dissolution was F5 that was produced with PEG6000. The dissolution data obtained was found to correlate well with the solubility data. The batches of SAs that exhibited better solubility were found to display better dissolution when compressed into tablets.

CONCLUSION

From the current investigations, it can be concluded that directly compressible SAs of ETX can be successfully produced by SA technique. The agglomerates drastically augmented flow properties of the drug and displayed better solubility that consequently enhanced the dissolution rate of the drug. Hence, agglomerates produced were able to be directly compressed on account of their enhanced flow properties and better compaction behavior. Therefore, SA can be a useful tool in formulation development of poorly compressible drugs. The SAs can finally be dispensed as capsules or compressed tablets as per the need.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

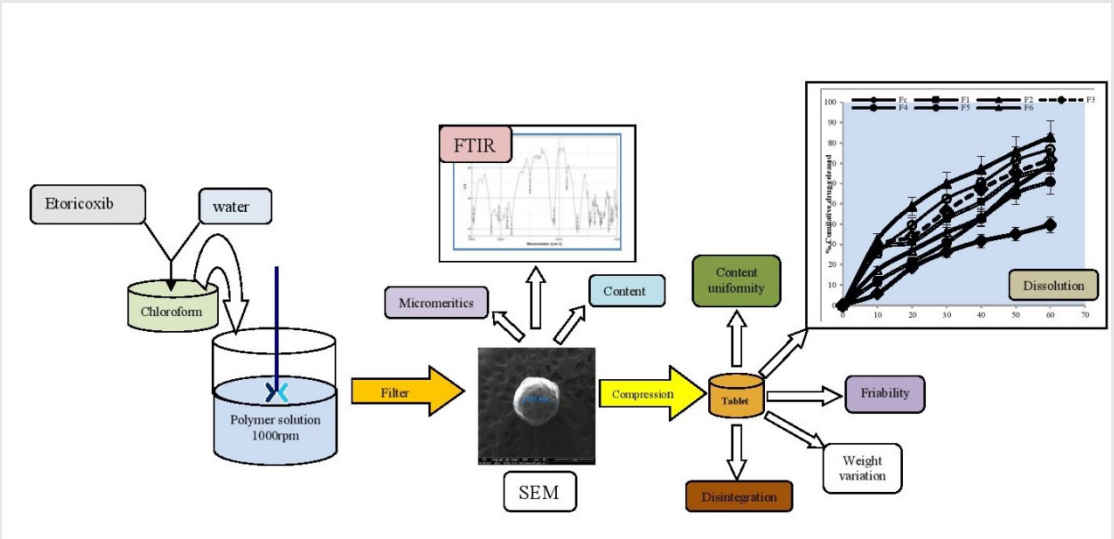
PVP K30: Polyvinylpyrrolidone K30; **PEG 6000:** Polyethylene Glycol 6000; **SA:** Spherical agglomeration;

SAs: Spherical agglomerates; **ETX:** Etoricoxib; **NSAID:** Nonsteroidal anti-inflammatory drugs; **QESD:** Quasi Emulsion Solvent Diffusion; **SEM:** Scanning Electron Microscopy; **FTIR:** Fourier Transform Infra-Red; **USP:** United States Pharmacopoeia; **IP:** Indian Pharmacopoeia.

REFERENCES

1. Yadav AV, Yadav VB. Designing of pharmaceuticals to improve physicochemical properties by spherical crystallization techniques. J of Pharm Res. 2008;1(2):105-12.
2. Chourasia MK, Jain NK, Jain S, Jain NK, Jain SK. Preparation and characterization of agglomerates of flurbiprofen by spherical crystallization technique. Indian J Pharm Sci. 2003;65(3):287-91.
3. Paradkar AR, Pawar AP, Jadhav NR. A novel particle engineering technique. Asian J Pharm. 2010;4:4-10.
4. Mahanty S, Sruti J, Niranjan PC, Bhanoji RME. Particle Design of drugs by Spherical Crystallization Techniques. Int J Pharm Sciences and Nanotechnology. 2010;3(2):912-4.
5. Kallies B, Konig A, Ulrich J. Solidification by crystallization in dropsm international workshop for industrial crystallization. Breman, Germany. 1993:138.
6. Kate P, Pe¯na R, Jonathan DT, Kanjakha P, Rachel S, Zoltan K. *et al*. Litster. Particle design via spherical agglomeration: A critical review of controlling parameters, rate processes and modelling. Powder Technology. 2018;326:327-43.
7. Wu S, Li K, Zhang T, Gong J. Size control of Atorvastatin Calcium particles based onSpherical Agglomeration. Chem Eng Technol. 2015;38(6):1081-7.
8. Maghsoodi M. Effect of process variables on physicomechanical properties of the agglomerates obtained by spherical crystallization technique. Pharm Dev Technol. 2011;16(5):474-82.
9. Alaa HS, Abdelfattah AA, Nermeen AE. Etoricoxib-loaded bio-adhesive hybridized polylactic acid-based nanoparticles as an intra-articular injection for the treatment of osteoarthritis. Int J Pharm. 2020;578:119081.
10. Arunkumar P, Indulekha S, Vijayalakshmi S, Srivastava R. Synthesis, characterizations, *in vitro* and *in vivo* evaluation of Etoricoxib-loaded Poly (Caprolactone) microparticles–a potential Intra-articular drug delivery system for the treatment of Osteoarthritis. J Biomater Sci Polym Ed. 2016;27(4):303-16.
11. Suruchi R, Brijesh SK. Transdermal delivery of Etoricoxib through ethosomal formulation: An ingenious approach towards treatment of skin inflammation. Journal of Drug Delivery Science and Technology. 2017;40:95-104.
12. Aulton ME. Pharmaceutics: The Science of Dosage form Design. 2nd ed. NewYork: Churchill Livingstone. 2002.
13. Patil SV, Sahoo SK. Spherical crystallization: A method to improve tabletability. Research J of Pharmacy and Technology. 2009;2(2):234-7.
14. Kangale P, Lohray BB, Mishra A, Davada P, Kini R. Formulation and optimization of porous osmotic pump based controlled release system of Oxybutinin. AAPS Pharm Sci Tech. 2007;8(3):E1-7.
15. Patel JK, Bodar MS, Amin AF, Patel MM. Formulation and optimization of mucoadhesive microsphere of Metaclopramide. Ind J Pharm Sci. 2004;66(3);300-5.
16. Das A, Nayak AK, Mohanty B, Panda S. Solubility and dissolution enhancement of etoricoxib by solid dispersion technique using sugar carriers. Research Article. 2011. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC 3263729/
17. http://www.scholarsresearch library.com
18. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. 2nd ed. Bombay: Varghese Publishing House. 1976;69.
19. Khan KA, Sarfaraz MD, Doddayya H. Design and evaluation of Aceclofenac fast dissolving tablets prepared by crystallo-co-agglomeration technique. Int J Pharm Pharm Sci. 2011;3(4):116-23.
20. Lieberman HA, Lachman L. Pharmaceutical dosage forms: Tablets. 2nd ed. New York: Marcel Dekker. 1990;299-333.

PICTORIAL ABSTRACT



SUMMARY

Spherical agglomerates of Etoricoxib were successfully prepared using ethanol as a good solvent, chloroform as a bridging solvent and water as a bad solvent for etoricoxib using different polymers like PVP K30 and PEG 6000. FTIR suggested the chemical integrity of the drug in the formulations. SEM studies indicated the agglomerates were discrete and spherical. Further, agglomerates containing polymers were thus found to display good micrometric properties, with improved solubility profile. Values of Carr's index and Hausner's ratio indicated that incorporation of polymers drastically helped in improving the micrometric properties. Spherical agglomerates compressed into tablets using talc and magnesium stearate exhibited better dissolution rate compared to the conventional tablets of etoricoxib. Thus, from the present study it can be concluded that Spherical Agglomeration technique can be an efficient tool to produce directly compressible, cost effective tablets of poorly compressible drugs like etoricoxib.

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