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RESEARCH ARTICLE

PARTICLE SIZE REDUCTION OF ACECLOFENAC BY USING SURFACTANTS AND MICRONIZATION FOR NANOCARRIER ENTRAPMENT

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ABSTRACT

The Aceclofenac (2-[(2, 6-dichlorophenyl) amine] phenylacetoxyacetic acid) is a Non-Steroidal Anti-Inflammatory category of drug, which is water insoluble drug of BCS class-II which has low solubility and high permeability phenomenon. The particle size reduction technique is used to solubilize the aceclofenac. The particle size of aceclofenac in bulk form is 140-200 microns. In this experiment, The 35 microns particle size was reduced in powder form from 140-200 microns by using Air jet mill and 17.08 microns size was reduced by using dynamill and 33.62 microns particle size was reduced by using Tween 80 as surfactant as considered as lowest particle size. The Labrasol and Na. CMC were also used in this experiment. The equipments used to reduce particle size of aceclofenac are ultra-Turrax (Ultra-sonication), Air jet mill and Dynamill. These all instruments used to reduce the particle size of aceclofenac are safe and not any chemical compound was added in any of the method described above. This study was used to see the uniform nature of the nano- and micro-particles entrapping the aceclofenac drug obtained by High shear homogenization, high pressure homogenization, Solvent-Diffusion evaporation and membrane contactor methods. If the particle size of aceclofenac cannot be reduced less than 14 microns then at the time of Permeation studies the same particle size will enter in Stratum corneum of Skin and entrapped in the carrier matrix. And formation of microns sized particles will obtained while preparing Solid lipid nanoparticles.

Keywords: Solubilization, Particle size reduction, Air jet mill, high shear homogenizer, particle size analyzer, Dynamill

Abbreviations: BCS shows Biopharmaceutical classification system, D.M.: Demineralised water, HSH: High speed homogenizer, Na. CMC: Sodium carboxy methyl cellulose, ACS: Aceclofenac solubility, I.P.: Indian Pharmacopoeia

INTRODUCTION

The Aceclofenac (2-[(2, 6-dichlorophenyl) amine] phenylacetoxyacetic acid) is an effective non-steroidal anti-inflammatory drug (NSAID) of phenyl acetic acid group, which possesses remarkable anti-inflammatory, analgesic and antipyretic properties¹. Aceclofenac appears to be particularly well-tolerated among the NSAIDs, with a lower incidence of Gastro-intestinal adverse effects². Unfortunately, Aceclofenac has low water solubility i.e. (0.058 mcg/ml) leading to poor dissolution. The biopharmaceutical classification system (BCS) divides all drug candidates into four different groups, according to their solubility and permeability³. Aceclofenac is an example of BCS class II compound,⁴ Therefore, the improvement of aceclofenac is an important issue for enhancing its bioavailability and therapeutic efficacy. Several techniques are commonly used to improve dissolution and bioavailability of poorly water-soluble drugs, such as Salt formation, pH adjustment, complexation and prodrug. All these have use of chemicals for their activity⁵. Objective of this research is to reduce the particle size of Aceclofenac to nanometer size by using Air jet mill, high speed homogenization containing surfactants (Tween 80, Labrasol and Na. CMC) and Dynamill.

MATERIALS

The Aceclofenac was a sample purchased from Suyash Laboratories. The Tween 80 was purchased from SD fine, India and Labrasol was purchased from Gattefosse SAS.

METHODS

Particle Size of Aceclofenac-The particle size of Aceclofenac was analyzed by Sympatec Particle size analyzer of bulk powder size reduction of Aceclofenac.

- 1. The lowest Particle size of Aceclofenac powder after Air jet mill⁵** = the three cycles of Air jet mill to reduce bulk original sized particles. The three readings were obtained as 1st cycle, 2nd cycle, and 3rd cycle. The average reading was taken as the minimum particle size can reduced after particle size reduction.
- 2. The Particle size of Aceclofenac in following Solvents-**The 3g drug was dispersed in 50g D.M. Water, 0.1 % Tween 80 was weighed and put in beaker. The stirring with high speed homogenization was done for 15 min. with 2 min. gap each at 13.500 rpm, where it was characterized with particle size. Then 100ml water was added, and the above solution was then divided into three parts. In 1st part 0.1 % Tween 80 was added and stirring with HSH was done for 10 min. In the 2nd part the 1% Labrasol was added and stirred with HSH for 10 min. at 6.500 rpm. In the 3rd part 10ml NaCMC was added and stirred for 10 min. with HSH at 6.500 rpm. Further stirring at high speed of 9500 for 10 min. and 13.500 for 10 min. The batches were coded as ACS-1.1, ACS-1.2, ACS-1.3 (where ACS denotes to Aceclofenac solubility)

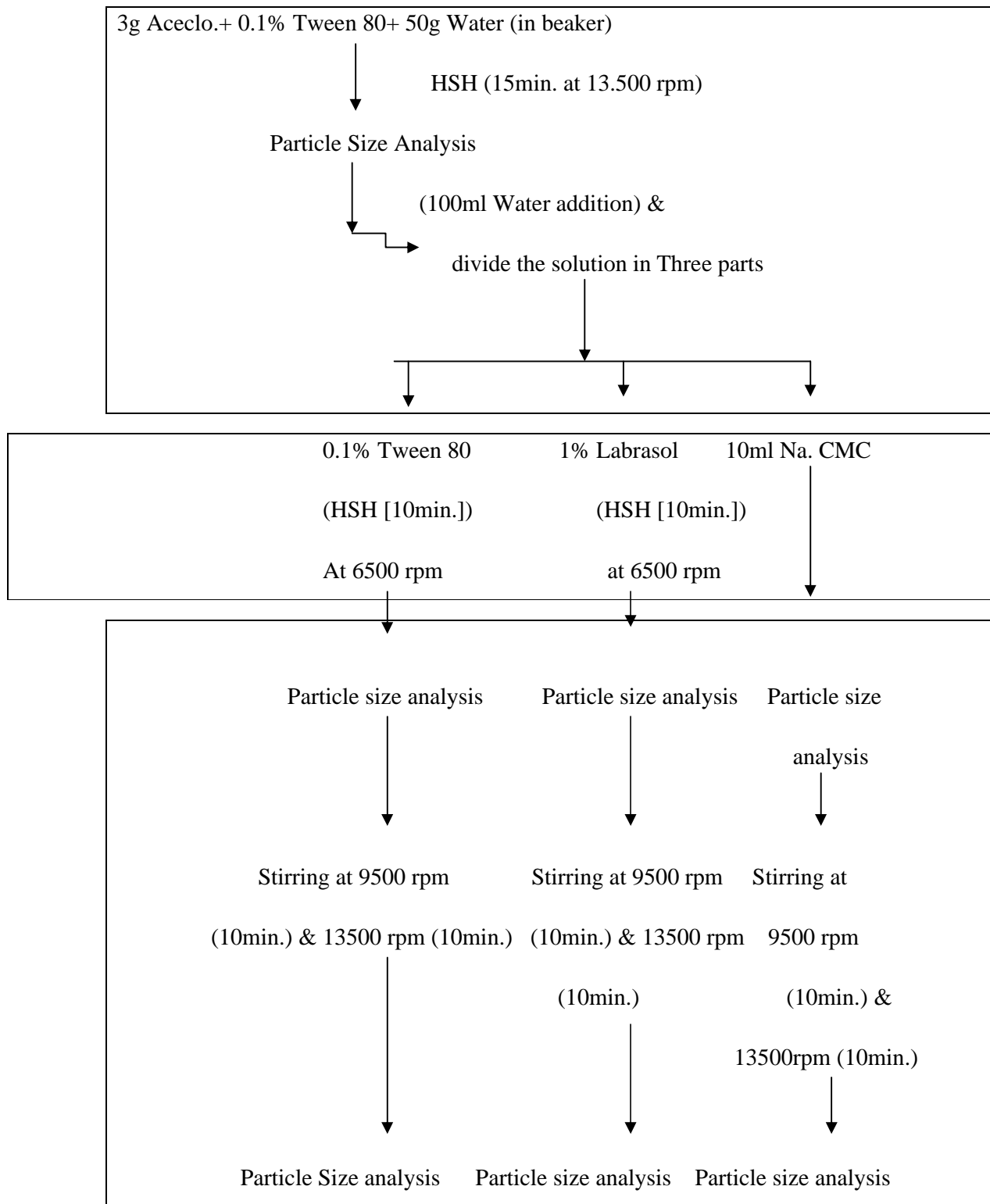


Figure 1: Flow chart of Processing of Particle size reduction by Surfactant mixture

3. Dynamill particle size reduction - The dynamill instrument was used to solubilize Aceclofenac in the water where tween 80 and Na. CMC were added by the time 45 min. at 13.500 rpm using zirconium beads of 0.2 mm dia. The batch was coded as ACS-1.4.

RESULTS

1. The Particle size of bulk Aceclofenac powder- 140-200 microns

2. The lowest Particle size of Aceclofenac powder after Air jet mill= the three cycles of Air jet mill to reduce 140-

200 microns sized particles. The three readings were size reduction in the Air jet mill of the Aceclofenac is 32 obtained as 1st cycle, 2nd cycle, and 3rd cycle. The minimum μm .

Table 1: Showing Particle size

Cycles	Particle Size (X_{90}) μm
1	37
2	34
3	33.6
4	32

Table: 2 Composition and particle size of Aceclofenac after solubilization with surfactants

Composition	Batch	Solvents to dissolve drug	Particle size (X_{90}) μm
Aceclofenac+Tween 80	ACS-1.1	Tween 80	58 (1), 33.62 (2)
Aceclo.+Tween 80+Labrasol	ACS-1.2	Labrasol	60 (1), 47.91 (2)
Aceclo.+Tween 80+Na CMC	ACS-1.3	Na. CMC	60 (1), 36.81 (2)
Dynomill	ACS-1.4	Tween 80, Labrasol, Na. CMC	17.08

Na. CMC: Sodium Carboxy-methylcellulose, (1) and (2) indicates the 1st cycle and 2nd cycle of the high speed homogenizer

Table: 3 Particle Size distributions of all batches for X_{10} , X_{50} , and X_{90}

Batch No.	X_{10} (μm)	X_{50} (μm)	X_{90} (μm)
ACS-1.1	2.27	13.41	33.62
ACS-1.2	7.72	27.01	47.91
ACS-1.3	2.78	15.27	36.81
ACS-1.4	4.48	10.6	17.08

DISCUSSION

The minimum particle size of the Aceclofenac after dissolved in surfactant solution and micronization was found 17.08 (X_{90}) μm by using dynamill. The Tween 80 (Batch 1.1) gives 33.62 μm (X_{90}), Labrasol (Batch 1.2) gives 47.91 μm (X_{90}) and Na. CMC (Batch 1.3) gives 36.81 μm (X_{90}) particle sizes. By adding all the surfactants (Batch 1.4) and applying pressure by dynamill which are zirconium beads with 2mm dia. So that Aceclofenac can be minimized till 17.08 μm (X_{90}) particle size as shown in Table 3. The Aceclofenac powder particle size is reduced from the 37 μm , 34 μm , 33 μm and 32 μm by 1st cycle of

Air jet mill, 2nd cycle of Air jet mill, 3rd cycle of air jet mill and 4th cycle of air jet mill as given in Table 1. The particle size discussed in the Table 2 was based upon the first cycle and second cycle which were referring to (1) and (2) respectively. The addition of surfactants and increase in stirring time was there in the following cycles. The values of particle size analyzer in this are 58 μm which is then reduced to the 33.62 μm in ACS-1.1, the 60 μm is reduced to 47.91 μm in ACS-1.2, 60 μm is then reduced to 36.81 μm in ACS-1.3.

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