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EVOLUTION AND MICROMERETIC CHARACTERIZATION OF DRUG ACECLOFENAC GRANULES

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1. ABSTRACT

Drug release was retarded with an increased in polymer concentration due to the gelling property of polymers. The *in-vitro* drug release from proposed system was best explained by the Higuchi's model indicating that the release of drug from tablets displayed diffusion controlled mechanism. The aim of this study was to improve the dissolution rate of Ibuprofen release the drug in controlled manner over a period of 24 h. Matrix tablets were prepared by direct compression method, using hydrophilic polymers (HPMC/ guar gum). Matrix tablets were prepared by wet granulation method using different concentration of hydrophilic polymers (HPMC/ guar gum).Tablets were evaluated for *in-vitro* drug release profile in phosphate buffer, pH 6.8, (without enzymes).Drug release was retarded with an increased in polymer concentration due to the gelling property of polymers. The *in-vitro* drug release from proposed system was best explained by the Higuchi's model indicating that the release of drug from tablets displayed diffusion controlled mechanism.

Key words-: Granules, Tablets, Bulk Density, Drug

2. INTRODUCTION

Most of the oral controlled drug delivery systems release the drug by diffusion, dissolution or combination of both mechanisms to release the drug in a controlled manner to the gastrointestinal tract. The physicochemical properties and biological properties of drugs the drug profile must be determined for the desired release rate of the drug from controlled release dosage form. The oral course is viewed as most regular, uncomplicated, advantageous and safe because of its simplicity of administration, and patient consistence. Dominant part of the pharmaceutical items intended for oral conveyance is prompt discharge or conventional release system for fast medicine captivation. Oral medication conveyance is the most broadly appropriate route among every single other route, for example, nasal, ophthalmic, rectal, transdermal and parenteral routes. It has been investigated for systemic transport of drug through different pharmaceutical products of a dissimilar dosage form. This is possible through administration of a conventional dosage form in a particular dose and at a particular frequency. The frequency of administration or

the dosing interval depends upon its half-life or mean residence time and its therapeutic index. In most cases, the dosing interval is much shorter than the half-life of the drug resulting in number of limitations associated with such a conventional dosage form. These limitations can be overcome by controlled release dosage forms. Oral route was the most convenient route for the drug delivery. It received more attention in the pharmaceutical field because of more flexibility in designing of dosage form than the drug delivery design for other routes. The design for oral route depends up on various factors such as type of delivery system, the disease being targeted, the patient, the length of therapy and the properties of drug. The oral course is viewed as most regular, uncomplicated, advantageous and safe because of its simplicity of administration, and patient consistence. Dominant part of the pharmaceutical items intended for oral conveyance is prompt discharge or conventional release system for fast medicine captivation. An ideal dosage regimen in drug therapy of any disease is the one which immediately attains the desired therapeutic concentration of drug in plasma (or at the site of action) and maintains it constant for the entire duration of treatment.

3. METHODOLOGY

3.1. Preparation method of tablet

The constant amount of drug was weighed and passed through sieve no.40. The equivalent amounts of polymers (HPMC/ guar gum), lactose was weighed, screened through screen sieve no.40. The screened mass was transferred into a clean and dry mortar and mixed gently for 5 min and alcoholic solution (IPA) of PVP K 30 (5% w/v) was gradually added to the powder mixture and blended to form a wet mass. The wet mass was passed through sieve no. 10 to form granules and resulting granules were placed on a tray for drying into the oven at 50°C for 10 min. The dried granules were passed through sieve no. 18. Corresponding amount of magnesium stearate and talc were weighed and mixed with granules for 3 min. Using a single station hand operated tablet compression machine granule were compressed to form tablets .

Table 3.1 Composition of the sustained release matrix tablets containing Aceclofenac.

Ingredients (mg)	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
Aceclofenac	200	200	200	200	200	200	200	200	200
HPMCK15M	50	100	150	200	-	-	-	-	100

Guar Gum	-	-	-	-	50	100	150	200	100
Lactose	200	150	100	50	200	150	100	50	50
PVP K30	25	25	25	25	25	25	25	25	25
IPA	q. s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Talc	20	20	20	20	20	20	20	20	20
Magnesium	5	5	5	5	5	5	5	5	5

3.3. Micromeretic characterization of granules

Determination of bulk density

Mass (M) of the powder divided by the bulk volume (Vb) gives Bulk density which expressed as g/cm^3 and depends on particle size distribution, particle shape and particles adhere. Apparent bulk density (ρ_b) was determined by pouring the blend into a 10 ml graduated cylinder [74]. The bulk density was calculated using folowing formula:

$$\rho b = \frac{M}{Vb}$$

Determination of tapped density

Tapped density was measured by a measuring cylinder containing a known mass (M) of powder blend and was tapped 100 times using density apparatus. The minimum volume (V_t) occupied by the powder in the cylinder was measured. The tapped density (ρ_t) was calculated using the formula.

$$\rho t = \frac{M}{Vt}$$

Determination of angle of repose

Angle of repose was determined using funnel method, powder blend was poured through a funnel which raised vertically a maximum cone height (h) [76]. Radius of the heap (r) was measured and angle of repose (θ) was calculated using the formula:

$$tan\theta = \frac{h}{r}$$

The values of angle of repose indicating flow properties have been recommended as <25 indicating excellent flow, 25-30 indicating good flow, 30-40 indicating passable, and value >40 indicated very poor flow of the powered material.

Determination of compressibility index

Compressibility index is the simplest way for measurement of flow property of powder to determine its compressibility. It is an indication of the ease with which a material can persuaded to flow which is calculated using following equation:

$$\text{Compressibility index}(\%) = \frac{\rho t - \rho b}{\rho t} \text{ X } 100$$

Where ρ_t is the tapped density, and ρ_b is the bulk density.

The values of compressibility index indicating flow properties have been recommended as <12 indicating excellent flow, 12 – 16 indicating good flow, 18 – 21 indicating fair to passable, 25 – 35 indicating poor, 33 – 38 indicating very poor, and value > 40 indicated extremely poor flow of the powered material.

Determination of Hausner's Ratio

Hausner ratio is an indirect index of ease of powder flow, density determinations were used to calculate the Hausner's ratio using following formula:

$$HR = \frac{\rho t}{\rho b}$$

Where ρt is tapped density, and ρb is bulk density.

Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (> 1.25).

RESULT AND DISCUSSION

4.1 Micromeritic properties

The flow property of prepared granules was estimated based on different micromeritic properties. The bulk density and tapped density was determined using USP bulk density apparatus and the results were represented in Table 4.6. The bulk density and tapped density were found to be almost similar, indicating similar flow properties,differences in both were very small indicating that the change volume is very less even after 100 tapping, which confirms uniform particle size range and reproducibility in drug content.

Table 4.6 Results of micromeretic characterization of aceclofenac granules.

Formulation code	Bulkdensity (g/cm^3)	Tapped density(g/cm^3)	Compressibility Index(%)	Hausner's Ratio	Angleofrepose (□)
F1	0.438±0.002	0.503±0.006	12.4±0.346	1.14±0.046	30.60±0.566
F2	0.429±0.007	0.479±0.009	12.65±0.618	1.12±0.040	30.00±0.173
F3	0.477±0.019	0.560±0.023	14.76±1.721	1.17±0.023	28.03±0.208
F4	0.491±0.010	0.551±0.013	10.93±0.150	1.12±0.003	28.30±0.346
F5	0.416±0.007	0.471±0.009	11.74±0.248	1.13±0.004	27.24±0.295
F6	0.412±0.027	0.479±0.018	14.0±1.212	1.16±0.015	26.78±0.600
F7	0.477±0.010	0.556±0.010	14.20±0.266	1.166±0.004	27.77±0.546
F8	0.466±0.003	0.541±0.001	14.05±0.531	1.623±0.064	27.29±0.272
F9	0.478±0.003	0.561±0.001	14.76±0.462	1.19±0.035	27.34±0.140

Hausner's ratio is related to inter-particle friction it is indirect measures of bulk density, size and shape, surface area, moisture content and cohesiveness of granules. A higher Hausner'sratio and more fine particles indicate greater cohesion between particles while a low range indicates good flowability. The desirable value of Hausner's ratio is <1.25 for good flow of materials, for granules it was found in range of 1.12±0.040 to 1.19±0.035 (Table

4.6). An increase in Hausner's ratio is due to increase in granule size and this might be due to increased void space between theparticles. It is well established that particle size and shape influences flowability, fine particles (<100 mm) tend to be more cohesive and therefore less free-flowing, whereas larger denser particles tend to be free-flowing. The rougher and more irregular the surface of the particles, the higher will be the angle of repose. Angle of repose of granules increased from 26.78±0.600 to 30.60±0.566 as the particle size increased, indicating the decrease in flowability of granules (Table 4.6) which is also supported by the results of Hausner's ratio study.

A high compressibility index is indicative of the tendency to form bridges between the particles, smaller the compressibility index better will be the flow properties. A value of 5 to 15 indicates excellent flow, 12 to 18 good flow, 19 to 21 fair flow, 22 to 35 poor flow, 36 to 40 very poor flow and >40 extremely poor flow. The results show that the granules had good and excellent flow property (10.93±0.150 to 14.76±0.462) (Table 4.6).

5. CONCLUSION

In the Micromeretic characterization of aceclofenac granules studies characterized based on its physiochemical properties by the determination of melting point, solubility, UV spectroscopy and FTIR studies. For quantitative assessment of Aceclofenac UV spectrophotometric method was established in the formulations. Linearity of calibration curve was observed in the range of 0-40 µg/ml. Drug polymer interaction studies were carried out for 4 weeks at 40±2ºC and 75±5% RH. The desirable value of Hausner's ratio is <1.25 for good flow of materials, for granules it was found in range of 1.12±0.040 to 1.19±0.035 (Table 4.6). An increase in Hausner's ratio is due to increase in granule size and this might be due to increased void space between theparticles. It is well established that particle size and shape influences flowability, fine particles (<100 mm) tend to be more cohesive and therefore less free-flowing, whereas larger denser particles tend to be free-flowing.

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