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Research Article

Effect of various binding agents on tablet hardness and release rate profiles of diclofenac sodium tablets

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ABSTRACT

Diclofenac sodium tablets were prepared by wet granulation method using starch and PVP K-30 as binding agents. Diclofenac sodium (DS) is a substituted phenyl-acetic acid derivative; widely used in the management of many inflammatory conditions. It also has analgesic and antipyretic actions. The effects of binding agents on the physical characteristics of the Diclofenac granules were studied. The granules were evaluated for angle of repose, bulk density, compressibility index etc. and showed satisfactory results. The tablets were subjected to weight variation test, drug content, hardness, friability and in vitro release studies. The in vitro dissolution study was carried out for one hour using United States Pharmacopoeia USP- 2 (paddle-type dissolution apparatus) in phosphate buffer (pH 7.4) as dissolution media. All the tablet formulations showed acceptable pharmacotechnical properties and complied with pharmacopoeial specifications. The results indicated that a decrease in release kinetics of the drug was observed with starch as binder than with PVP K-30. The mechanical and release properties of Diclofenac sodium tablets formulated with povidone (PVP) and starch as binders were studied and compared. A good correlation between various physical parameters of granules and tablets was observed. The PVP-K30 showed better binding properties compared to the starch (potato).

Keywords: polyvinyl pyrrolidone k-30; starch (potato); Diclofenac sodium.

INTRODUCTION

"Conventional tablets" is our everyday tablet a powder that's pressed together into a solid mass.The tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness, and ease in manufacturing. In wet granulation process the surface polarity of both powder and polymer binders are important factors in determining the strength of granules. Binders and powder with similar surface polarities produce strong granules and the degree of polymerization increases the strength of granules. (Horisawa, E., 1993; Sinchalpanld, N. 1993)

Diclofenac sodium (DS) is a substituted phenyl-acetic acid derivative; widely used in the management of many inflammatory conditions. Diclofenac sodium is poorly soluble in water and acidic pH (1-3) but is rapidly soluble in alkaline pH (5- 8). Clinically, nonsteroidal anti-inflammatory drugs (NSAIDs) are the most frequently prescribed by physicians for inflammatory disorders. NSAIDs exert their effect through inhibition of cyclooxygenase-II, the main form of isozyme associated with inflammation. But the simultaneous inhibition of cyclooxygenase- I and the resulting gastric and renal dysfunction limit their frequent use.

Polyvinylpyrrolidone (PVP) is used widely as a binding agent for pharmaceutical tablets. It is a commonly used inactive ingredient in the preparation of pharmaceutical products. It serves as a dry and damp binding substance in the production of granules and tablets, as well as a thickening agent and solubizer.

PVP-K30 possess high binding strengths, they are suitable for the wet granulation and direct compression of tablets. Granules prepared by using PVP were found to be stronger and less friable compared with the methocel, acacia and methyl cellulose (Joneja S.K 1999; Cutt T., Fell., 1986).

Potato starch BP is the most commonly used excipient in the manufacture of tablets. It has been used as disintegrant, fillers or as binders (Gilbert S. Banker, 2nd Edition, 1990; Kottke MK 1992).

Binders are added to tablet formulation to impart plasticity and thus increase the inter particulate bonding strength within the tablet (Uhumwangho MU 2004). By promoting plastic deformation, binders increase the degree of consolidation or compactions while decreasing the brittle fracture tendency (capping and lamination) during tableting (Itiola AO, Pipel N, 1986).

The objective of this study is to evaluate the various physical characteristics of granules and tablets formulated using PVP-K30 and starch. In the present study,

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Table 1: Composition of diclofenac sodium tablets using different binding agents

S.No	Ingredients	Formula (mg/tablet)	
		F1	F2
1.	Diclofenac Sodium	100	100
2.	Lactose Mono hydrate	170	170
3.	SSG	30	30
4.	Povidone K30	-	10
5.	Starch(potato)	10	-
6.	IPA(Isopropyl alcohol)	q.s	q.s
7.	Magnesium Stearate	04	04
TOTAL		314mg	314mg

we have investigated the influence of some binders on the tablet hardness and dissolution studies of Diclofenac sodium tablets.

MATERIALS AND METHODS

DS was obtained as a gift sample from Win Medicare Ltd, Modipuram, and Uttar Pradesh, India. Crospovidone (PVP K -30), Sodium starch glycol ate (SSG) and were gifted sample from Cipla, Kurkumbh,India, Lactose monohydrate, Magnesium stearate was procured from S.D Fine Chemicals, Mumbai, India, were used and all other chemicals/solvents used were analytical grade.

PREPARATION OF GRANULES

Wet granulation method was used to prepare tablets (Zafar Iqbal Roohullah *2003*). Formulation with Different binders was compressed into tablets. The required quantities of Diclofenac sodium, Lactose monohydrate, SSG (disintegrant) were weighed accurately using analytical balance and were mixed well using laboratory conditions. Accurately weighed quantity of binder (PVP K30) was then dispersed in IPA (Isopropyl alcohol) and stirred well. The binder solution was then slowly incorporated into the above mixed powder to obtain a damp mass. The damp mass was passed through a granulating sieve # 16 to obtain the granules. Then the granules were dried in a hot air oven at 40 ^{0}C temperature less than the temperature of all the ingredients used. The dried granules were passed through sieve #22 in order to obtain the uniformed sized granules. All the granules were lubricated with magnesium stearate and compressed using single punch in a multistation compression machine (CEMACH), which is equipped with 8mm concave edge punches.

Evaluation of tablet formulations

1. PRE COMPRESSION PARAMETERS

a) Angle of repose (θ): The angle of repose (tan θ) was determined by cone angle method (Parrott.EL.SaskiW,1977).The accurately weighed powder was taken in a funnel. The height funnel (h) was adjusted in such way that the tip of the funnel just touches the apex of the heap of the powder. The powder was allowed to flow thorough the funnel freely on to the surface. The diameter of the powder cone(r) was measured and angle of repose was calculated using the following equation (Ritala, M 1987)

$$\theta = \tan^{-1} \frac{h}{r}$$

D) Bulk density

An accurately weighed sample (M) of granules was carefully added to graduated cylinder through a funnel (Aulton M.E., 1998). Apparent bulk density (ρb) was determined by placing pre-sieved drug excipients blend into a graduated cylinder and measuring the volume (V_b) and weight (M) “as it is”.

Bulk density =Weight of powder/Bulk volume

E) Tapped density

The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density (ρt)

Table 2: Physical properties of diclofenac sodium tablets prepared by using different binding agents

Formulation	Angle of repose (degrees)	Carr’s index	Hausner’s ratio	Bulk density
F1	23°.34'	15.40	1.225	0.303
F2	20°.41'	14.78	1.231	0.304

Table 3: Physical properties of diclofenac sodium tablets prepared by using different binding agents

Formulation	Average weight (mg)± SD	Hardness (kg/cm2) ± SD	Friability %±SD	Weight variation (mg)
F1	314± 1.2	6.5 ± 0.1	0.639	315.2 to 312.8
F2	314± 2.0	5.0 ± 0.1	0.710	316 to 312

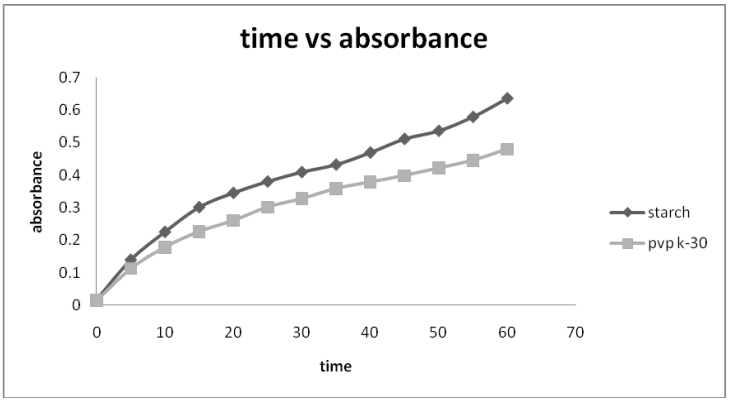

Figure 1: *In vitro* Dissolution profile of diclofenac sodium tablets using different binding agents

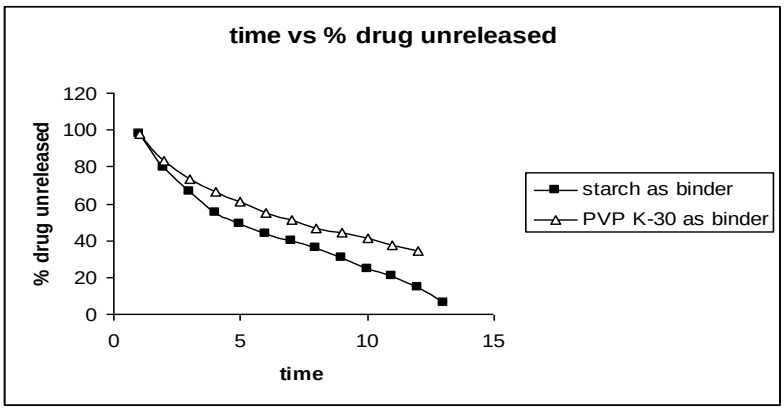

Figure 2: First Order Plots of diclofenac sodium by using different binding agents

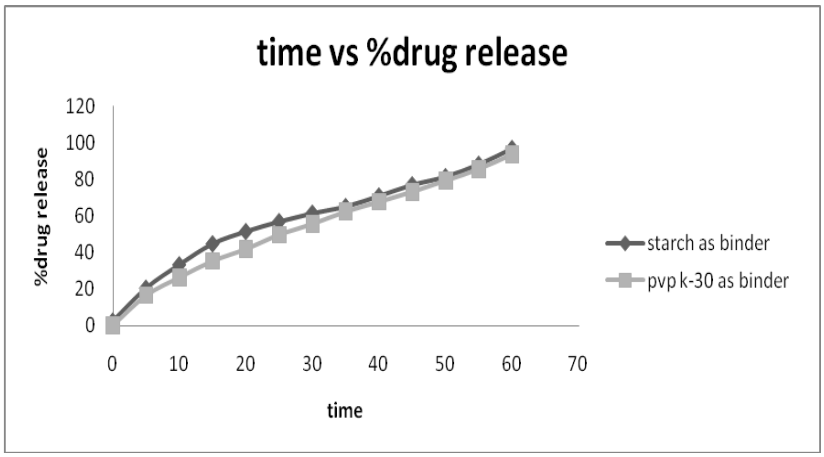

Figure 3: First Order Plot of diclofenac sodium by using different binding agents

was calculated using following formula.

Tapped density = Weight of powder /Tapped volume

b) Compressibility index (I): Compressibility an indication of the ease with which a material can be induced to flow and is given by %compressibility which was calculated from the bulk and tapped density.

Carr's index = (Tapped density – Bulk density / Tapped density) * 100

C) Hausner's ratio: Hausner's ratio is an index of ease of powder flow. It was Calculated by following formula (Lachman L, Lieberman HA 1987).

Hausner's Ratio = Tapped density / Bulk density

2. POST COMPRESSION PARAMETERS

A) Weight variation test: The percentage weight variations for all formulations were shown in Table No.3. Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. In all formulations, the tablet weight is more than 600 mg , hence 5% weight variation is allowed (Ritala, M., 1987)(Martin A 2001).

b) Hardness test for tablet

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablet was determined using Pfizer hardness tester it is expressed in kg/cm^2.Three tablets were randomly picked and hardness of the tablet was determined (Ritala, M., 1987)(Martin A 2001).

C) Friability test

The friability (Ritala, M., 1987) (Martin A 2001)of tablets was determined using Roche Friabilator. It was expressed in percentage (%) 10 tablets were initially weighed ($W_{initial}$) and transferred into Friabilator. The Friabilator was operated at 25 rpm for 4 min run up to 100 revulsions. The tablets were weighed again (W_{final}) the % friability was then calculated by –

$$\% \, Friability = \frac{Before\ Friability - after\ Friability}{Before\ Friability} \times 100$$

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable (Indian pharmacopoeia volume-II,1996).

***INVITRO* DISSOLUTION STUDY**

In vitro dissolution study was performed by taking six tablets of each formulation and average of six results was considered as percentage drug release. The dissolution studies were carried out up to one hour for all the formulations using *the United States pharmacopoeia* (USP) apparatus II (Paddle method) taking 900 ml of dissolution medium using pH 7.4 phosphate buffer. The rotational speed of the paddle was set at 50 RPM at 37 ± 0.5^{o}C. The 5 ml of aliquots were withdrawn at predetermined time interval for every 5 minutes by replacing a fresh sample of dissolution medium. The absorbance of the collected samples was measured using UV- spectrophotometry at λ max of 276nm (Remington Volume-I 21st Edition).

RESULTS AND DISCUSSION

Diclofenac sodium tablets were prepared by wet granulation process. Precompressional studies were carried out before compression of the tablet. The flow property of the granules were studied and was found to be in the prescribed limits according to I.P. and the results were shown in the table 2. The results of other pre compressional studies were shown in the table 2 such as Carr's index, Hausner's ratio and Bulk density. The post evaluation of the tablets were been performed according to official and non official books and the results were placed in table 3. The evaluations of the tablets were done in triplicate in order to get accuracy of the results. The hardness and the friability of the Diclofenac tablets were in the range 6.5 kg/cm^2, 5 kg/cm^2 and 0.63 %, 0.71 % respectively.

The drug content estimation has been performed according to I.P. and was observed at 276nm. The same tablets were subjected to the dissolution for the estimation of the release rate and it was found to be 96.8% 93.6% for starch and povidone respectively, with in a 60 min time period.

Both the binding agents which were used in the formulation process were of 10%. Due to the high binding property of the tablets formulated with povidone has given a less release of the drug when compared to starch.

SUMMARY AND CONCLUSION

From the present study it can be concluded that povidone k-30 (10%) may be used as a binding agent in the tablet formulation when high mechanical strength is more essential. Tablets prepared with 10% povidone k-30 and starch was found to be ideal for the preparation of uncoated tablets. Since they both displayed good tabletting characteristics and have high potentials for substitution for other more extensive binders.

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