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Formulation and Evaluation of Aceclofenac Oral dispersible Tablets in the design *Hordeum Vulgare Hull*

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Abstract
In the present study, Oral dispersible Tablets were designed with a view to enhance patient compliance. In this method, the *Hordeum Vulgare Hull*, cross carmellose sodium, and sodium starch glycolate were used as superdisintegrants (4 and 6%), along with microcrystalline cellulose and mannitol, to enhance mouth feel. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water absorption ratio and *invitro* dipersion time. Based on the in vitro dispersion time, the formulations were tested for the *in vitro* drug release patterm. Tablets having *Hordeum Vulgare Hull* showed the release profile comparable to those tablets having sodium starch glycolate and cross carmellose sodium.
Keywords: Oral dispersible tablet, *Hordeum Vulgare Hull*, *In vitro* dissolution study, sodium starch glycolate.

Contents

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1. Introduction
Excipients are additives used to convert active pharmaceutical ingredients into a suitable doageforms. New and modified excipients continue to emerge with a better drug deliveryw and modified excipients continue to emerge with a better drug delivery perfoemance. Excipients of natural origin areof particu lar intrest to formulation scientists because of their reliability and sustainability. I recent years natural substances have evoked tremendous intrest due to theor pharmacutical applications, such as their diluent, binder and disintegrant qualities in tablets. Plant product are therefore an attrative alternative to synthetic products because of biocompatibility, low toxicity, and low price, compared to synthetic products. Excipients from natural are also generally non-polluting renewable sources for the sustainable supply of cheaper pharmaceutical products[1].

Difficulty in swallowing is a common problem of all age groups especially geriatic and pediatric patients, due to the physiological changes associated with these groups tending towards non-compliance and ieffective therapy. Recent advances in novel drug delivery systems (NDDS) have aimed to enhance the safety and efficacy of drug molecules

by formulating a convenient dosage form for administration and they have also aimed to achieve better patient compliance. One such approach is a fast disintegrating tablet. Advantages of this drug delivery system include accuracy of dosage easy portability it is an alternative to the liquid dosageforms and is ideal for pediatric and geriatric patients with a rapid onset of action[2].

The present was carried out tostudy the disintegrant property of *Hordeum vulgare* hull in comparison with cross carmellose sodium by formulating fast disintegranting tablets. Aceclofenac was used as a model drug in the formulations. The concept of formulating Oral dispersible Tablets offered a suitable and practical approach for serving the desired objective of faster disintegration and the dissolution characteristics with potential incresed bioavailability.

2. Materials and Method

Hull was collected from the seeds of the *Hordeum vulgare* (fam: Poaceae), which was purchased from the local market and treated suitably. The seeds were authenticated by botanical survey of India, jodhpur. Microcrystalline cellulose was purchased form Ases Chemicals Jodhpur and Sodium starch glycoalate was purchased from Loba Chemiw Pvt Ltd Mumbai. All other chemicals and reagents were of analytical grade.

Collection, Isolation and Treatment of Hull

The seeds of the *Hordeum vulgare* having the complete hull were pucased form the local market and moistened with the mixture of water and ethanol for 4 to 60 minutes. Next the damp seeds with the hull were crushed in an iron pestle mortar with mild impact. The content were air dried and then the outer hull was separated and colleted. The collected hull was subjected to grinding in an electric grinder and passed through sieve No. 100. The powder was percolated with 70% ethanol for 48 hours and the alcohol was collected with continuous addition of fresh menstrum untill o more pink color appeared[3]. The hull was initially dried for 12 hours at room temperature and then for 48 hours at 50^{o}C. The dried hull powder was stored in an air tight container.

Preparation of fast dissolving tablets

Different tablet batches (AODS1, AODS2, AFDH3, AFDH4, AFDC5, & AFDC6) were prepared as per the formula given in Table 1. All the ingredients were passed through the # 60 mesh separately. Acccurately weighed quantities of aceclofenac, microcrystalline cellulose, mannitol and other excipients were mixed in geometrical order. This blend was granulated with an alcoholic solution of PVP (10% w/v in 50% ethanol) and passed through a #22 mesh, and lubricated with talc & magnesium stearate. The granules were evaluated for various parameters and the results are summarized in Tablet 2. The tablets were compressed using 9mm round concave punches to get tablets of 300mg weight on eight station rotary tablet machines (Hardik Engineering, Ahmedabad)

Evaluation of granules

The granules of all the batches were evaluated for different parameters like bulk density, tapped density, carr's index, Hausner ratio, and angle of repose. Bulk density and tapped density were determined using the bulk density apparatus. A pre weighed quantity of granules was transferred to the measurung cylinder were subjected to 100 tappings and the tapped was calculated.

Carr's index and Hausner ratio

Carr's index and Hausner ratio of the granules was calculated using the following formulas (Dt-Db) * 100/Dt and Dt/Db, respectively. Where Dt was the bulk density of the granules and Db was the tapped density of the granules[4]. The angle of repsoe indicated the flow property of granules. The granules were subjected to flow through a funnel and a pile was obtained. The angle of repose was calculated using the following formula [$\tan \theta = h/r$], where θ was the angle of repose and h and r were the height and radius of the pile, respectively.

Evaluation of tablets

Twenty tablets were randomly selected from each batch and indivdually weighed. The average weight of theseselected tablets was calculated, and the individual tablet weight was compared with the average tablet weight[5]. The thickness and crushing strength of the tablets were measured by using the vernier Caplipers and Monsanto hardness tester, respectively. A tablets hardness of 4-5 kg was considered adequate for mechanical stability. All the determinations were made in triplicate and the average value was calculated.

Fribility

The friability test was performed to assess the effect of friction and shocks, which could often cause the tablet to chip cap or break. The fiability at 25 rpm for four minutes. The weight of 20 tablets before and after completion of the test was recorded and the friability and after completion of the test was recorded (Wo-W) *100/Wo, where Wo is the weight of tablets before rotation and W is the weight of tablets after rotations. All the determinations were made in triplicate and the average value was calculated[6].

Drug content uniformity

For the drug content uniformity test ten tablets were weighed and powdered. The powder, equivalent to 25 mg Aceclofenac was taken in a 100 ml volumetric flask and dissolved in methanol. The voulme was made upto the

mark with methanol. The volume was made upto the mark with methanol[7]. From this solution, ml was withdrawn, diluted to 100ml with methanol, and was filtered through Whatman No. 40. The drug content in the filtrate was determined by measurung the absorbance at 275 nm. The mean percent drug content was calculated as an average of thress determinations.

Wetting time

The wetting time of the tablets can be measured using a simple procedure. A pieces of tissue paper folded twice was paced in a glass petridish of 10 cm internal diameter and 10ml of amaranth solution was added to the petrisish. A tablet was placed carefully on the surface of the tissue paper. The time required for water to reach the upper surface of the tablet is noted as the wetting time[8]. All the determinations were made in triplicate and the average value was calculated.

Water absorption ratio

A pieces of tissue paper folded twice was placed in a glass petridish of 10cm internal diameter and 10ml of amaranth solution was added to the petridish. A pre-weighed tablet was placed carefully on the suface of the tissue paper. After complete wetting the tablet was again weighed. The water absorption ratio was determined by the following formula (Wb-Wa)* 100/Wa. Where was the weight of the tablet before water absorption and Wb wa the weight of the after water absorption. All the determinations were made in triplicate and the average value was calculated[9].

***In vitro* dispersion time**

Three tablets per batchwere evaluated for *In vitro* dispersion time. For determination of invtiro dispersion time, one tablet was placed in a beaker containg distilled water, at 37±0.5^{o}C, and the time required for the complete dispersion was determined[10].

***In vitro* dissolution study**

In vitro dissolution of the Oral dispersible Tablets was studied in United State Pharmacopeia dissolution testing apparatus II (Electrolab TDT08L), emplying a paddle stirrer at 50 rpm using 500 ml of Phosphate uffer (PH 6.8), at 37^{o}C ± 0.5^{o}C, as the dissolution medium. one tablet was used in each test. Aliquots of the samples were withdrawn at each time travel was replaced with a fresh dissolution and analyzed for drug content by measuring the absorbance at 242.5nm, using a UV/VS spectroscopy (CECILCE-7400)[11].

Stability testing

Short term stability studies on the promising formulations (AODS2, AFDH4 & AFDC6) were carried out by storing the tablets in an amber coloured rubber stoppered vial at 40^{o}C/75% RH over a perid of 45 days[12]. At the interval of 15 days, the tablets were visually examined for anyphysical changes in drug content and invitro dispersion time.

3. Results and Discussion

Oral dispersible Tablets were prepared by the wet granulating technique employing *H. vulgare* hull, sodium starch glycoalate, and cross carmellse sodium as superdisintegrants, in different concentrations along with microcrystalline cellulose. Mannitol was used as a diluent in the formulation. A total of six formulations were designed prepared and evaluated. For each designed formulation the granules were evalutated for micrometric properties shown in Table 2. Bulk density was found to between 0.284 & 0.354 gm/cm^3 & Tapped density between 0.320 & 0.409 gm/cm^3, for all formulation from the density data, the carr's Index was calculated & was found to be with in the range of 15.01 to 13.21%. The value of the range of repose was found to be in the range of 30.76 & 28.50^{o}C, showing a good flow property of granules[13]. The Hausner ratio was found to be 1.2 for all the formulations.

The prepared tablets of all the formulations processed suffucient hardness in the range of 5.0 to 5.2 kg/cm^2. The percent friability below 1% was an indication of the good mechanical resistance of the tablets. As the granules were free flowing (angle of repose 30^{o}C – 40^{o}C & Carr's Index <15%) the tablets obtained were of uniform weight, with a acceptable variation vaiations as per Ipspecifications that is below ± 7.5%. All the formulations containing hull was showing very fast disintegrating when compared with those formulations having sodium starch glycolate. The drug content was found to be in the range of 92.91 to 98.73% which was with in accepatable limits. Although the water absorption ratio for the AFDH3 & AFDH4 batches[14]. Were found to be more than 55% the wetting time for these formulations was found to be much higher when compared to the wetting time of those formulation having Sodium starch glycolate & cross carmellose sodium as super disintegrating.

In vitro dissolution studies on all the formulations were carried out in the phosphate buffer (PH = 6.8) various dissolution parameters values of the % drug dissoluted in 5,10,15 & 30 mints are shown in Table 4 & the dissolution profiles depicted in Fig 1. This data also reveals that the formulations AFTS4 displays almost similar results that the formulations AFTS1 & AFTS2. Short term stability studies of the formulations AFTS 2, AFTS4 & AFTS6 are represented in Table 5-7. Indicate that there are no significant changes in drug content & Invitro dispersion time at the end of 45 days[15]. Over all formulation AFTS 3 & AFTS 4 CONTAING H. Vulagre hull (4% w/w & 6% w/w

respectively) & 35% w/w micro crystalline cellucose were found to be promising & have shown an invitro dispersion time of approcimately 36 sec & 33 sec respectively. The experiments data also revelas that the results obtained from the H. Vulgare hull are comparable & even slightly better the those of sodium starch glycolate & cross carmesllose sodium.

Table 1. Composition of different batches of Oral dispersible Tablets

Ingredients (mg/tablet)	Batch codes					
	AODS 1	AODS 2	AFDH 3	AFDH 4	AFDC 5	AFDC 6
Aceclofenac	20	20	20	20	20	20
Micro crystalline cellulose	100	100	100	100	100	100
Sodium starch glycolate	10	15	----	-----	-----	----
Hull	------	------	10	15	-----	-----
Cross carmellose sodium	------	------	------	------	10	15
Mannitol qs	120	115	120	115	120	115
Total tablet weight	250	250	250	250	250	250

*All batches contained 10% polyvinylpyollidine in ethyl alcoholas a binder and 2% talc and 1% magenism stearate, AODS1, AODS2 formulations containg sodium strch glycolate as a superdisintegrants, AFDH3, AFDH4: formulating containing *H. Vulgare* hull as a super disintegrating, AFDC5, AFDC6 formulation containing cross carmellose sodium as a superdisintegrat.

Table 2. Evaluation of Granules

Parameters*	Batch codes					
	AODS 1	AODS 2	AFDH 3	AFDH 4	AFDC 5	AFDC 6
Bulk density (gm/cm3)	0.284	0.276	0.252	0.260	0.354	0.354
Tapped density (gm/cm3)	0.320	0.305	0.300	0.315	0.40	0.409
Carr's index	15.01	13.62	14.10	15.27	8.07	13.21
Hausner ratio	1.18	1.16	1.16	1.18	1.11	1.16
Angle of repose	30.76	33.47	29.49	29.55	28.10	28.50

*Average of three determinations.

Table 3. Evaluations of Tablets

Parameters*	Batch codes					
	AODS 1	AODS 2	AFDH 3	AFDH 4	AFDC 5	AFDC 6
Thickness (mm)	4.30	4.30	4.52	4.56	4.67	4.6
Friability (%)	0.25	0.38	0.40	0.45	0.39	0.51
In vitro dispersion time (sec)	40±3.5	34±1.72	35.6±1.51	32.4±1.51	33.3±2.00	28.6±1.10
Hardnes (kg/cm2)	5.0±0.25	4±0	5.2±0.25	3.50±0.28	4.0±0	4.66±0.28
Wetting time (sec)	25.30±2.4	24.33±1.2	47.33±2.6	47.33±2.6	16±1.0	28±2.5
Waterabsorption ratio (%)	125.80	127.40	65.43	66.14	105.25	108.65
% drug content	98.73±0.30	95.17±0.64	96.05±0.1	94.60±0.27	92.91±0.19	97.15±0.85
Weight variation (%)	280-300 (mg with I IP limits of ±7.5%)					

*Average of three determinations

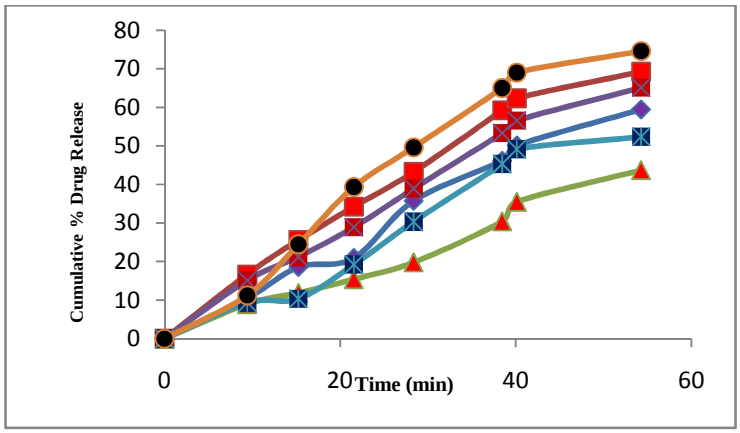

Figure 1. *In vitro* cumulative drug release versus time profiles. Plots showing percent cumulative drug release in 0.1 N HCL from AODS1 Formulation; AODS2 Formulation; AFDH3 Formulation; AFDH4 Formulation; AFDC5 Formulation; AFDC6 Formulation

Table 4. *In vitro* release profile of drug

Formulation code	Percent drug release			
	A5	**A10**	**A15**	**A30**
AODS 1	35.78	77.18	79.65	95.51
AODS 2	40.61	70.77	82.30	93.84
AFDH 3	32.76	60.69	78.21	88.10
AFDH 4	42.54	71.41	85.81	94.26
AFDC 5	66.70	67.48	68.54	87.13
AFDC 6	40.52	76.45	80.91	86.54

AODS1, AODS2: Formulation containing sodium starch glycolate (4 and 6%, respetively) as a superdisintegrates, AFDH 3, AFDH 4: Formulation containing *H.Vulgare* hull(4% & 6%, respetively) as a superdisintegrants, AFDC5, AFDC 6: Formulation containing cross carmellose sodium (4 and 6% respectively) as a superdisintegrants. A5: Percent drug released in 5 minutes, A10: Percent drug released in 10 minutes, A15: percent drug released in 5minutes, A20: percent drug released in 30 minutes.

Table 5. Stability data of AODS 2 forulation at 40°C/75% RH

Time (Days)	Physical changes	% drug content ±SD*	*In vitro* dispersion time ± SD*
1 (initial)	----------	95.17±0.54	34.0±1.6
15	No Changes	96.03±0.25	34.4±1.3
30	No Changes	95.92±0.43	34.5±1.3
45	No Changes	95.67±0.67	35.4±1.6

*Average of three determinations mean percent drug content on the first day is 95.17±0.54 on days is 95.67±0.67, with the difference between day 45 and the first day being 0.41

Table 6. Stability data of AFDH2 formulation at 40°C/75% RH

Time (Days)	Physical changes	% drug content ±SD*	*In vitro* dispersion time ± SD*
1 (initial)	----------	96.06±0.1	33.1±1.5
15	No Changes	97.74±0.35	33.4±2.0
30	No Changes	97.74±0.65	33.9±1.4
45	No Changes	96.15±0.51	34.2±1.6

*Average of three determinations mean percent drug content on the first day is 96.06±0.1on days is 45 is 96.15±0.51, with the difference between day 45 and the first day being 0.41

Table 7. Stability data of AFDC 2 formulation at 40°C/75% RH

Time (Days)	Physical changes	% drug content ±SD*	*In vitro* dispersion time ± SD*
1 (initial)	----------	98.51±0.85	28.6±1.1
15	No Changes	97.31±0.65	30.2±1.4
30	No Changes	97.14±0.80	10.6±1.1
45	No Changes	96.15±0.86	30.7±1.5

*Average of three determinations mean percent drug content on the first day is 98.51±0.85 on days is 45 is 96.15±0.86, with the difference between day 45 and the first day being 0.54

4. Conclusion

Finally I concluded that the Oral dispersible Tablets contain the crospovidone and sodium starchglycolate exhibited good flow and compression characteristics. AFDC5 tablets containing coprocessed super disintegrants exhibited quick disintegration and improved drug dissolution. It can be concluded from the present work that co-processed superdisintegrants of cross carmelose sodium & Micro crystalline cellulose are the mainly used in the AFDC5 fast dissolving tablets.

5. Acknowledgement

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