SHORT COMMUNICATIONS

Formulation and Dissolution Rate Studies on Dispersible Tablets of Ibuprofen

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Dispersible tablets of ibuprofen were formulated employing potato starch, Primogel, microcrystalline cellulose (MCC) and pregelatimised starch (PGS) and the tablets were evaluated for content of active ingredient, hardness, friability, disintegration time, uniformity of dispersion and dissolution rate. Tablets formulated employing Primogel as internal and external disintegrant and tablets formulated employing potato starch as internal disintegrant and Primogel and PGS as external disintegrants fulfilled all the official and other requirements of dispersible tablets. These tablets also gave rapid and higher dissolution rate then the formulated as well as conventional (commercial) tablets. The dissolution of ibuprofen from the tablets followed first order kinetics. The dissolution rate of ibuprofen, a poorly soluble drug could be increased by formulating it as dispersible tablets.

Dispersible tablets are uncoated tablets that produce uniform dispersion in water[1]. They should disintegrate within 3 min and produce a uniform dispersion that passes through mesh No. 22 when dispersed in water. Dispersible tablets are formulated for paediatric use as an alternative to suspensions. Ibuprofen is a widely used antiinflammtory, analgesic drug, which is practically insoluble in water[2]. Tablets (400, 200 mg) and suspensions containing 100 mg of ibuprofen per 5 ml are available commercially. No dispersible tablets formulations of ibuprofen are presently available. In the current work dispersible tablets of ibuprofen were formulated and evaluated for various characteristics including dissolution rate. The possibility of increasing the dissolution rate of ibuprofen through the formulation of dispersible tablets was also investigated.

Ibuprofen was a gift sample from M/s. Veco Pharma Ltd., Visakhapatnam. Pregelatinised starch was prepared from potato starch in the laboratory by a known method[3]. Primogel (sodium starch glycollate) and microcrystalline cellulose (Avicel) were gift samples from M/s. Aristo Pharmaceuticals Ltd., Mumbai.

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Potato starch, I.P. (Loba-chemie), Lactose, I.P. (S.D. Fine Chem), Talc, I.P. (Loba-chemie), Magnesium stearate, I.P. (Loba-chemie) and two brands of Ibuprofen (200 mg) tablets were procured from local market.

Dispersible tablets each containing 100 mg of ibuprofen were prepared as per fomulae given in Table-1 by conventional wet granulation method. Pregelatinised starch, microcrystalline cellulose, potato starch (dry) and Primogel were tried as disintegrants. Starch paste was used as binder. The wet granules (mesh No. 12) were dried at 50° for 6 h. The dried granules were sized through mesh No. 16 and blended with external disintegrant and lubricants. Tablet granulations were compressed into tablets to a hardness of 5-7 kg/sq.cm. on Cadmach tablet machine. In each case 3 batches of 100 tablets each were prepared.

Disintegration times were determined in Thermonik Tablet Disintegration Test Machine I.P/B.P/USP standard using distilled water as the fluid. Hardness of the tablets was tested using Monsanto hardness tester. Friability of the tablets was determined in Friability Test Machine. All the tablets were tested for uniformity of dispersion as per I.P.

TABLE 1 : COMPOSITION OF PREPARED IBUPROFEN DISPERSIBLE TABLETS

Ingredient (mg/tablet)	Formulation						
	T1	T2	T3	T4	T5	T6	T7
Ibuprofen	100	100	100	100	100	100	100
Potato starch	100	—	—	—	50	50	50
Primogel	—	25	—	—	12.5	—	—
MCC	—	—	100	—	—	50	—
PGS	—	—	—	100	—	—	50
Lactose	225	340	265	265	302.5	265	265
Starch (as paste)	15	15	15	15	15	15	15
Talc	10	10	10	10	10	10	10
Magnesium stearate	10	10	10	10	10	10	10
Total Weight (mg)	500	500	500	500	500	500	500

TABLE 2 : DISINTEGRATION AND DISSOLUTION CHARACTERISTICS OF IBUPROFEN TABLETS

Formulation	D.T. (min-Sec.)	T_{50} (min.)	DE_{30} (%)	K1 x 10^2 (min^{-1})
T1	1 - 58	15	43.45	2.10
T2	2 - 52	6	62.97	5.55
T3	12-00	>30	12.09	0.70
T4	3 - 15	45	17.62	1.73
T5	2 - 13	3	84.74	19.27
T6	4 - 18	19	39.76	4.80
T7	2 - 20	4	78.00	13.18
C1	4 - 10	19	41.76	2.93
C2	6 - 20	33	20.13	2.60

Ibuprofen contents were estimated by measuring absorbance at 221 nm in phosphate buffer of pH 7.2. The method obeyed Beer's law in the concentration range of 0.5-10 µg/ml. Excipients used in the tablets did not interfere in the method. When a standard drug solution was assayed repeatedly (n=6), the coefficient of variation (precision) and relative error (accuracy) of the method were found to be 0.8% and 0.5% respectively.

The dissolution rate of ibuprofen from the tablets was studied in phosphate buffer of pH 7.2 using a USP XXI Dissolution Rate Test Apparatus employing paddle stirrer. As the tablets are rapidly disintegrating and dispersing into fine particles, paddle stirrer was found more suitable than basket stirrer. In each test one tablet containing 100 mg of ibuprofen, a speed of 100 rpm and a temperature of 37 ± 1° were employed. A 5 ml aliquot of

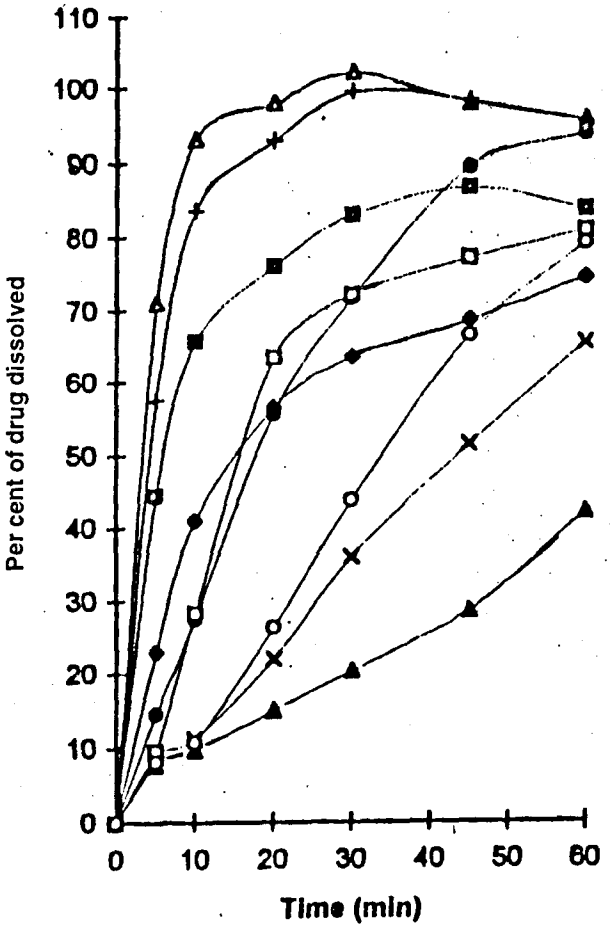

Fig. 1: Drug release profiles of various ibuprofen tabelts formulated (T1-T7) and commercial (C1, C2)

Disintegrants used in various formulations were as follows: Potato starch in T1 (—●—), Primogel in T2 (—■—), MCC in T3 (—▲—), PGS in TA (—x—), Potato starch and Primogel in T5 (—△—), Potato starch and MCC in T6 (—●—) and potato starch and PGS in T7 (—+—), C1 (—□—) and C2 (—○—) are two commercial brands of ibuprofen 200 mg tablets

dissolution medium was with drawn through a filter (0.45 μ) at different time intervals, suitably diluted and assayed spectrophotometrically at 221 nm for ibuprofen. For comparison, the dissolution rate of ibuprofen from two conventional tablets of ibuprofen was also studied.

Tablet formulations T1, T2, T3 and T4 were prepared employing potato starch, Primogel, MCC and PGS as disintegrants respectively. In each case half the amount of disintegrant was added before granulation (internal disintegrant) and the remaining half was added after granulation (external disintegrant). Another series of tablets were formulated employing potato starch as internal disintegrant and Primogel, MCC and PGS as external disintegrants in tablet formulations T5, T6 and T7 respectively.

All the tablets formulated were found to contain ibuprofen within 100 ± 5% of the labelled claim. Hardness of the tablets was found to be in the range of 5-6 kg/sq.cm and was found satisfactory. Friability of all the tablets was less than 1%. Tablet formulations T1, T2, T5 and T7 disintegranted within 3 min, complying the official (I.P.) disintegration time requirement of dispersible tablets. In the test for uniformity of dispersion, tablet formulations T2, T5 and T7 complied the official (I.P) requirement. The dispersion produced in water with these tablets passed through mesh No. 22, whereas with all other tablets about 10-40% of the tablet mass was trained on mesh No. 22. Thus tablets formulated employing Primogel as internal and external disintegrant (T2) and the tablets formulated employing starch as internal disintegrant and Primogel (T5) and PGS (T7) as external disintegrants fulfilled all the requirements of dispersible tablets.

Dissolution of ibuprofen from all the tablets formulated was studied in phosphate buffer of pH 7.2. This dissolution medium is specified in I.P[4] for the dissolution rate test of ibuprofen tablets. Dissolution of ibuprofen from all the tablets followed first order kinetics. Plots of log per cent remaining Vs time were found to be linear ('r' in the range 0.949 - 0.993). From the slopes of linear plots the dissolution rates were calculated. Dissolution efficiency (DE_{30}) values were calculated as suggested by Khan[5]. The dissolution parameters of various tablets are summarized in Table-2. Tablet formulations T2, T5, T7 gave rapid and higher dissolution rate of ibuprofen when compared to the other formulated as well as commercial conventional tablets. Based on DE_{30} values the following order of increasing dissolution was observed with various tablets.

Based on dissolution rate the following order of increasing dissolution was observed with various tablets.

T5>T7>T2>T6>C1>C2>T1>T4>T3

Tablet formulations T2, T5, T7 fulfilled all the requirements of dispersible tablets and also gave rapid and higher dissolution rates when compared to other tablets formulated and conventional (commercial) tablets.

Thus dispersible tablets of ibuprofen could be formulated employing Primogel as internal and external disintegrant and also with Potato starch as internal Primogel and PGS as external disintegrants. These tablets fufilled all official (I.P) requirements of dispersible tablets and gave rapid and higher dissolution rates and dissolution efficiency values than the conventional tablets. Dissolution rate of ibuprofen, a poorly soluble drug, could thus be increased by formulating it as dispersible tablets.

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Preparation and Evaluation of Submicron Cellulose Particulate System Containing Etoposide

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Cellulose derivatives have been used to prepare nanospheres entrapping the drug etoposide. Adopting the technique of desolvation for nanosphere formation, discrete spheres have been obtained, as observed by transmission electron microscopy. Study on *in vitro* release profile of sample batches showed bi-phasic release pattern.

Some of the unique features like satisfactory stability, easy preparation, possibility of reducing toxicity and elevating the therapeutic efficacy, make nanoparticle a suitable drug-delivery system for targeted distribution of anti-cancer drugs[1]. Nanoparticles containing cytotoxic agents could be useful for the treatment of certain cancers that often show resistance to the uptake of free drug[2]. The feasibility of this approach was demonstrated by many of the investigators and many of the applications to which liposome have been put, await investigation using nanoparticles[3]. Tissue biocompatibility of cellulose derivatives has been studied recently[4].

In our present study, we have made an attempt to identify the suitability and potentiality of ethyl and methycellulose as a natural carrier for anticancer drugs through their *in vitro* release characteristics. The preliminary investigation on release characteristics of this system may enable to justify its *in vivo* application in targeted distribution of anti cancer drugs. Hence, discrete and uniform nanospheres containing etoposide have been prepared from ethyl and methylcellulose by modified desolvation method. The drug loading capacity and *in vitro* release characteristics of these nanospheres were studied.

Etoposide B.P. was obtained from Cipla, Bangalore. Ethyl cellulose 20,064-6 and methylcellulose 27,444-5 were purchased from Aldrich Chemicals, USA. Other reagents like sodium sulfate anhydrous, ethyl acetate and sodium phosphate were of analytical grade.

Nanospheres were prepared by modified desolvation method reported previously by Mukherji et al[5], where

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