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Formulation and Evaluation of Nimesulide Dispersible Tablets Using Natural Disintegrants

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Dispersible tablets of nimesulide (DTN) were formulated using natural substances as disintegrants such as *Plantago ovata* seed husk, *Cassia tora* (Sickle senna) and *Cassia nodosa* in different concentrations. Formulations were evaluated for the standards of dispersible tablets and were compared with marketed products. It was observed that all the formulations were acceptable with the reasonable limits of standards required for dispersible tablets.The study revealed that natural gums used as disintegrants were effective in low (5%) concentration.

Ispaghula husk consists of dried seeds of the plant known as *Plantago ovata*. It contains mucilage, which is present in the epidermis of the seeds[1-5]. The mucilage is used as binding agent in the granulation of material for preparation of compressed tablets. *Plantago ovata* seed husk has high swellability[6] and gives uniform and slightly viscous solution hence it is used as a suspending and thickening agent[7-8]. Some other material such as *Cassia tora* and *Cassia nodosa*[9-12], which are non toxic in nature, have nutritional value and used in the food material, showed the same behaviour at low concentration as *Plantago ovata* seed husk.

The present investigation was carried out to prepare dispersible tablets of nimesulide[13-14] (DTN) using *Plantago ovata* seed husk (Ispaghula), *Cassia tora* and *Cassia nodosa* as disintegrants, to establish the standards required for the dispersible tablets, to optimize the effective concentration of the disintegrant and to compare the formulations with marketed products.

EXPERIMENTAL

Nimesulide was obtained from Nicholas Piramal (India) Ltd., Pithampur. Lactose and talc were procured from Loba-chemie, Mumbai. Magnesium stearate was obtained from S.D. Fine Chemicals Ltd., Biosar. Ispaghula husk 100 g package was procured from local market. The ispaghula husk was dried at 50°, mixed and powdered and passed through sieve no. 100. Cassia tora and Cassia nodosa seeds were procured from local market. These seeds were dried at 50° for 24 h and then powdered and treated similarly as in case of ispaghula husk. Other materials used in the formulation and evaluation were of pharmacopoeial grade.

Preparation of Dispersible Table[15-16]:

Dispersible tablets of nimesulide (DTN) were prepared using disintegrants-ispaghula husk and seeds of *Cassia tora* and *Cassia nodosa* (pre-treated as mentioned previously) in 5, 10 and 15% concentration in each formulation. The composition of formulation is given in Table 1. The ingredients were thoroughly mixed and passed through sieve no. 22. Granules thus obtained were compressed using Cadmach single punch tablet compression machine and punch set an appropriate compression pressure (5-8 kg/cm^2).

Evaluation of DTN:

Dispersible tablets were evaluated under these parameter such as, weight variation, hardness, friability loss, disintegration time, drug content uniformity and dispersion patterns. Disintegration time was determined using a Thermonic Tablet Disintegration Test Apparatus, USP

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TABLE 1 : FORMULATION OF DISPERSIBLE TABLETS OF NIMESULIDE (DTN)

Ingredients mg/tab.	Formulae of DTN								
	NI_1	NI_2	NI_3	NCT_1	NCT_2	NCT_3	NCN_1	NCN_2	NCN_3
Nimesulide	100	100	100	100	100	100	100	100	100
Lactose	117.5	105	92.5	117.5	105	92.5	117.5	105	92.5
Ispaghula	12.5	25	37.5	-	-	-	-	-	-
Cassia Tora	-	-	-	12.5	25	37.5	-	-	-
Cassia nodosa	-	-	-	-	-	-	12.5	25	37.5
Talc	10	10	10	10	10	10	10	10	10
Magnesium Stearate	10	10	10	10	10	10	10	10	10

Where NI is DTN with Ispaghula, NCT is DTN with *Cassia tora* and NCN is DTN with *Cassia nodosa*.

TABLE 2 : EVALUATION DATA OF DTN

Formulation	Hardness Kg/sq.cm ±SD (n=6)	Friability (%) ±SD (n=5)	Wt. variation (%) (using 20 tab.)	Drug content ±SD (n=3)	Disintegration time (sec)
Marketed DTN	4.5±0.022	0.5±0.001	2.0	99.5±0.018	102
Conventional tablet (NM)	6.8±0.019	0.3±0.015	1.0	99.5±0.027	204
NI1	4.2±0.022	0.8±0.001	4.0	98.0±0.011	45
NI2	4.0±0.101	1.5±0.027	4.5	97.5±0.027	47
NI3	4.6±0.027	2.0±0.019	4.0	95.0±0.029	60
NCT1	5.0±0.008	0.6±0.022	4.5	95.0±0.022	35
NCT2	5.4±0.017	1.5±0.065	6.0	96.0±0.027	60
NCT3	5.2±0.021	1.0±0.053	4.5	94.0±0.001	60
NCN1	4.8±0.091	2.0±0.034	3.0	93.0±0.019	40
NCN2	5.2±0.110	3.0±0.019	3.8	94.5±0.091	45
NCN3	4.6±0.082	3.5±0.027	5.5	93.5±0.011	75

Where DTN is Dispersible tablet of nimesulide; NM is nimesulide; NI is DTN with Ispaghula, NCT is DTN with *Cassia tora*; NCN is DTN with *Cassia nodosa* and SD is Standard Deviation.

(Veego, India) using distilled water as a disintegration medium. Each formulation was tested for uniform dispersion as per official standards. (One tablet was placed in a beaker containing 25 ml of distilled water at 37±2°. After disintegration beaker was shaken and this fluid was passed through the sieve no. 22. Hardness of the tablet was tested, using a Pfizer hardness tester and friability by Roche Friabilator. Drug content was determined using UV-spectrophotometer (Shimadzu-140 A) at 295 nm. The evaluation parameters were shown in Table 2.

TABLE 3 : *IN VITRO* STUDY OF SELECTED DTN

Formul-tions code	Time (min)	Dissolution Efficiency (%)	Concentration of drug dissolved (mg)	Undissolved concentration of drug (mg) M	M_0 1/3-M1/3	Hixson Crowell cube root dissolution rate constant g. 1/3/min
N_1	0		0.0	M_0 = 0.0980	-	-
	2		0.0225	0.0755	0.0384	0.0192
	4	86.22	0.0465	0.0515	0.089	0.0225
	6		0.0635	0.0345	0.136	0.0226
	10		0.0845	0.0135	0.223	0.0223
NCT_1	0		0.0	M_0 = 0.0950	-	-
	2		0.0250	0.0700	0.0441	0.0220
	4	84.75	0.0445	0.0505	0.0866	0.0216
	6		0.0610	0.0340	0.1324	0.0220
	10		0.0805	0.0145	0.2125	0.0212
NCN_1	0		0.0	M_0 = 0.0930	-	-
	2		0.0220	0.0710	0.0390	0.0195
	4	82.79	0.0385	0.0545	0.0740	0.0185
	6		0.0590	0.0340	0.1290	0.0215
	10		0.0770	0.0160	0.2010	0.0201
MDTN	0		0.0	M_0 = 0.0995	-	-
	2		0.0120	0.0780	0.0369	0.0184
	4	79.89	0.0395	0.0605	0.0716	0.0179
	6		0.0588	0.0412	0.1187	0.0197
	10		0.0795	0.0205	0.1904	0.0190
MCTN	0		0.0	M_0 = 0.0995	-	-
	5	56.28	0.0350	0.0650	0.0581	0.0116
	10		0.0560	0.0440	0.1110	0.0111

Where, MDTN is Marketed Dispersible tablet of nimesulide and MCTN is a marketed conventional tablet of nimesulide.

Dissolution studies of DTN:

Dissolution studies were performed using a Dissolution Test Apparatus USP XXII. (Basket assembly) at 100 rpm using 900 ml of phosphate buffer (pH-7.4) and temperature was maintained at 37±0.5° through out the study. Ten milliliters of the sample was withdrawn at regular intervals and replaced with an equal volume of phosphate buffer. Samples were filtered (Millipore filter) and drug content was estimated by an UV-spectrophotometer (Shimadzu-140A) at 295 nm. All dissolution studies were carried out in triplicate. Cube root dissolution rate constant were determined using dissolution data and applying Hixson-Crowell cube root law[19]. Dissolution datas were shown in Table 3.

RESULTS AND DISCUSSION

The drugs content of the formulation was in the range of 100±15%. The hardness of the tablet was found to be 3.5-6.5 Kg/cm^2. Friability was observed to be less than 1% except in NCT_3 and NCN_3. All the formulations were

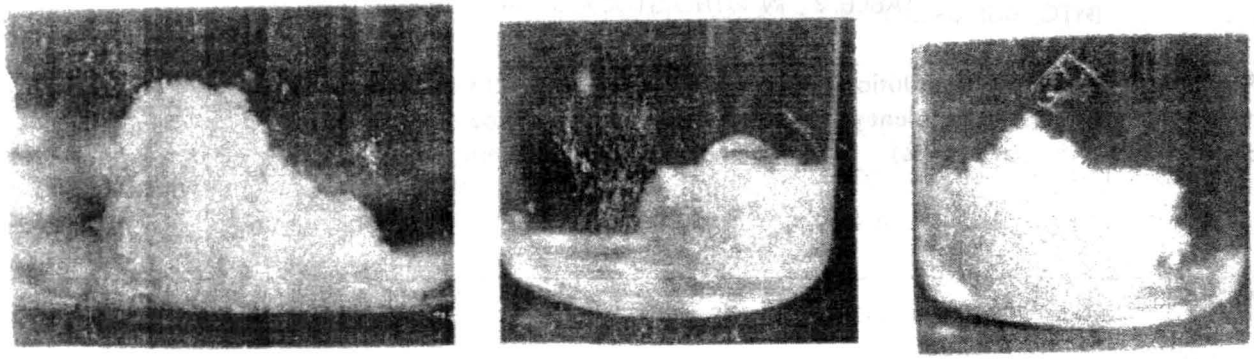

Fig 1 : Disintegration pattern of DTN after 90 secs

(a) DTN contained Ispaghula husk (b) DTN contained *Cassia tora* (c) DTN contained *Cassia nodosa*

disintegrated within 45-120 seconds. Disintegration pattern of the NI_1 NCN_1 and NCT_1 showed satisfactory and uniform dissolution Fig. 1. Other formulations though had all the characteristics of dispersible tablet, failed in uniform dispersion test. It may be due to higher swellability responsible for increased consistency resulting in poor dispersion. The study reveals that formulations prepared by using 5% natural disintegrants (NI_1 NCN_1 and NCT_1) exhibited good dissolution and uniform dispersion characteristics, necessary for the dispersion tablet as compared to marketed, conventional and dispersible tablets of nimesulide. All these formulation also followed Hixson-Crowell cube root dissolution equation and showed dissolution efficiency i.e. 82.16%, while the marketed products has 74.47%. This shows the formulation had better dissolution and dispersion characteristics.

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REFERENCES

1. Baveja S.K. and Gupta, B.M., **Indian J. Pharm.,** 1968, 30, 187.
2. Baveja, S.K. and Gupta, B.M., **Indian J. Pharm.,** 1968, 30, 247.
3. Mithal, B.M. and Kasid, J.L., **Indian J. Pharm.,** 1964, 26, 316.
4. Mithal, B.M. and Gupta, V.D., **Indian J. Pharm.,** 1965, 27, 331.
5. Chambers, W.P., **Quart. J. Pharmacol.,** 1948, 21, 44.
6. Levy, G. and Schawartz, T.M., **J. Am. Pharm. Assoc.,** 1958, 47, 471.
7. Patel, R.P., and Raghunathan, Y., **Indian J. Pharm.,** 1959, 21, 141.
8. Cheeke, P.R. and Schull, L.R. Eds., In; Natural Toxicants in Feeds and Poisonous Plants, Avi Publishing Co., Connecticut, USA, 1985, 191.
9. Grant, G., More, L.J., Mckenzie, N.H. and Pusztai, A., **J. Sci. Food Ag.,** 1982, 33, 1324.
10. Grant, G., More, L.J., McKenzie, N.H., Stewart, J.C. and Pusztai, A., **Br. J. Nutr.,** 1983, 50, 207.
11. Liener, I.E., Eds., In; Nutritional Significance of Lectins in the diet, Academic Press, New York, USA, 1986, 527.
12. Grant, G., **Progress Food Nutrition Sci.** 1989, 13, 317.
13. Magni, E., **Drugs,** 1993, 46, 10.
14. James, E. and Reynolds, F., Eds., In; Martindale, The Extra Pharmacopoeia, 29th Edn., The Pharmaceutical Press, London, 1989, 31.
15. Choudhari, K.P.R., Radha Rani, A. and Srilatha L., **The Eastern Pharmacist,** 1998, 163.
16. Choudhari, K.P.R. and Rama Rao, N., **Indian Drugs,** 1998, 36, 368.
17. United States Pharmacopoeia, Vol. XXII, USP Convention, Rockville, 1990, 1578.
18. Wurster, D.E. and Taylor, P.W., **J. Pharm. Sci.,** 1965, 54, 169.
19. Hixson, A. and Crowell, J., **Indian Eng. Chem.,** 1931, 23, 923.