Indion 414 as Superdisintegrant in Formulation of Mouth Dissolve Tablets

PURNIMA AMIN*, NAMITA PRABHU AND ANITA WADHWANI
Pharmaceutical Division, University Institute of Chemical Technology, Matunga, Mumbai-400 019, India.

The present research paper introduces Indion 414, an ion exchange resin, as a new superdisintegrant for pharmaceutical dosage forms. Indion 414 is a pharmaceutical grade weak acid cation exchange resin. Model drugs belonging to various classes were taste masked and formulated into palatable mouth dissolve tablets. Experiments were carried out to evaluate the disintegrant property of Indion 414 by incorporating Indion 414 in fast disintegrating dosage form like mouth dissolve tablets. Indion 414 was compared with the conventional disintegrants to determine its relative efficacy.

Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology[1,2]. Not all fast dissolving technologies actually dissolve; some use different disintegration mechanisms such as high levels of disintegrants[3,4] and/or effervescent agents that cause the dosage form to disintegrate rapidly in the patient's mouth within a minute and can be gulped easily without the need of water. Thus, it offers increased patient compliance and convenience. The present work was aimed to formulate and evaluate efficacy of Indion 414 in formulation of palatable fast disintegrating dosage form like mouth dissolve tablets. Mouth dissolve tablets are dosage forms, which when placed in the mouth, disintegrate or dissolve in the saliva within a minute without the aid of water or chewing[5]. Indion 414 is a high-purity pharmaceutical grade weak acid cation exchange resin available as a dry powder in potassium form. It is manufactured in an FDA-approved manufacturing facility. The parent material is manufactured in an ISO 9001 and ISO 14001 certified facility. Indion 414 is safe for oral consumption, cost-effective and is easily available. The advantages of ion exchange resins as superdisintegrants as compared to conventional ones are that they swell on getting hydrated but do not dissolve or have an adhesive tendency, a feature commonly encountered with gums. Thus the tablet disintegrates evenly. Ion exchange resins are efficient at considerable lower levels than recommended for conventional disintegrants. They facilitate the compression phase by conferring greater hardness to the tablets[6]. Ion exchange resins work equally efficiently with hydrophilic and hydrophobic formulations, especially with the latter where the conventional disintegrants are ineffective[6].

***For correspondence**
E-mail: dramin@vsnl.net

Indion 414 appears as a white-to-pale coloured powder, free from foreign matter. It is insoluble in water and in common solvents. Its matrix is made of cross-linked acrylic copolymer and is available in potassium form with carboxylic acid functional group. The specifications of Indion 414 are as given in Table 1. For effective disintegration of the tablet, 0.5 to 2% of Indion 414 is recommended. The advantages of Indion 414 as a tablet disintegrant include remarkable swelling tendency on wetting, thus causing rapid disintegration; there is no lump formation on disintegration; and it is compatible with commonly used therapeutic agents and excipients. Indion 414 does not stick to punches and dies.

Indion 414 was obtained as a gift sample from Ion Exchange India Ltd, Mumbai. Excipients for tablets were gifted by Signet Chemical Corporation, Mumbai. All solvents used were of analytical grade and were purchased from S. D. Fine Chemicals, Ltd, Mumbai.

The drugs selected for the study were roxithromycin, dicyclomine hydrochloride and montelukast sodium.

TABLE 1: SPECIFICATIONS FOR INDION 414

Parameter	Specification
Particle size distribution	
Retained on 100 BSS mesh	1% maximum
Retained on 100 BSS mesh	30% maximum
Moisture content	10% maximum
Sodium content	0.2% maximum
Potassium content	20.6 to 25.1%
pH of 10% slurry	7-9
Iron content, as Fe	100 ppm, maximum
Heavy metals, as Pb	20 ppm, maximum
Arsenic content	3 ppm maximum

Roxithromycin, chemically erythromycin 9 [o-(2-methoxy-ethoxy)-methyl-1]–oxime, is a macrolide antibiotic, widely used in the treatment of mild to moderate infections of the ear, nose and respiratory tract. Dicyclomine hydrochloride is an antispasmodic agent. Montelukast Sodium is an oral antiasthmatic agent. Bitter drugs like roxithromycin and dicyclomine hydrochloride were taste masked using ion exchange resins. The complexes along with the diluent were granulated with PVP K29/32 in Isopropyl alcohol. The wet mass was screened through 16 mesh and dried at 60° for 30 min. The dried granules were then screened through 40 mesh. Indion 414 was added extragranularly. Excipients were screened through 60 mesh. The blend was then compressed on a Cadmach single-stroke punch machine to give tablet weight of 460 mg[7] containing 50 mg of roxithromycin per tablet, and 200 mg containing 20 mg of dicyclomine hydrochloride respectively. Various formulations were tried to achieve a palatable formulation. Optimized formulations are as shown in Tables 2 and 3.

Montelukast Sodium, an antiasthmatic agent, was geometrically mixed with excipients including Indion 414 and the blend was directly compressed on a Cadmach single-stroke punch machine. The tablet weight was fixed at 150 mg. Each tablet contained montelukast sodium equivalent to 5 mg of montelukast. Optimized formulations are shown in Table 4.

The tablets were evaluated for various quality control parameters like appearance, taste, mouth feel, hardness, weight variation, *in vitro* dispersion time, *in vivo* dispersion time, drug content and drug release. Hardness of the tablets was determined with a Monsanto hardness tester. One tablet was placed in a beaker containing 6 ml of water. The time required for uniform dispersion of tablet was noted. *In vivo* dispersion time was determined by placing tablet in the mouth. The results of evaluation of the optimized formulations are depicted in Table 5.

Swelling index of the superdisintegrants was studied in simulated saliva. One gram of each sample was

TABLE 2: FORMULATION OF ROXITHROMYCIN MOUTH DISSOLVE TABLETS AND COMPARISON OF INDION 414 WITH EXISTING SUPERDISINTEGRANTS

Ingredients	F1	F2	F3	F4
	mg/tab	mg/tab	mg/tab	mg/tab
Roxithromycin: Indion 204 complex	330	330	330	330
Sodium saccharin	3	3	3	3
Monoammonium glycerrhizinate	3	3	3	3
Aspartame	15	15	15	15
PVP K29/32	20	20	20	20
Indion 414	10	-	-	-
Croscarmellose sodium	-	10	-	-
Sodium Starch Glycolate	-	-	10	-
Crospovidone	-	-	-	10
Avicel PH 101	59	59	59	59
Menthol	2	2	2	2
Mixed fruit flavor	6	6	6	6
Talc	6	6	6	6
Magnesium stearate	3	3	3	3
Aerosil	3	3	3	3

F1 is optimized formulation of Roxithromycin mouth dissolve tablets containing Indion 414. F2, F3 and F4 are different formulations tried with other superdisintegrants like Croscarmellose sodium, Sodium Starch Glycolate and Crospovidone.

TABLE 3: FORMULATION OF DICYCLOMINE HYDROCHLORIDE MOUTH DISSOLVE TABLETS AND COMPARISON OF INDION 414 WITH EXISTING SUPERDISINTEGRANTS

Ingredients	F5	F6	F7	F8
	Mg/tab	Mg/tab	Mg/tab	Mg/tab
Dicyclomine Hydrochloride: Indion 204 (O) complex	80	80	80	80
Sodium saccharin	5	5	5	5
Aspartame	8	4	4	4
PVP K29/32	20	20	20	20
Avicel PH 101	63	63	63	63
Strawberry flavour	6	6	6	6
Indion 414	10	-	-	-
Croscarmellose sodium	-	10	-	-
Sodium Starch Glycolate	-	-	10	-
Crospovidone				10
Talc	4	4	4	4
Magnesium stearate	2	2	2	2
Aerosil	2	2	2	2

F5 is optimized formulation of Dicyclomine hydrochloride mouth dissolve tablets containing Indion 414. F6, F7 and F8 are different formulations tried with other superdisintegrants like Croscarmellose sodium, Sodium Starch Glycolate and Crospovidone.

TABLE 4: FORMULATION OF MONTELUKAST SODIUM MOUTH DISSOLVE TABLETS AND COMPARISON OF INDION 414 WITH EXISTING SUPERDISINTEGRANTS

Ingredients	F9	F10	F11	F12
	mg/tab	mg/tab	mg/tab	mg/tab
Montelukast Sodium (equivalent to 5 mgof Montelukast)	5.19	5.19	5.19	5.19
Aspartame	4	4	4	4
Talc	4	4	4	4
Aerosil	2	2	2	2
Magnesium stearate	2	2	2	2
Indion 414	5	-	-	-
Croscarmallose sodium	-	5	-	-
Sodium Starch Glycolate	-	-	5	-
Crospovidone				5
Avicel PH 102	123.31	123.31	123.31	123.31
Menthol	0.5	0.5	0.5	0.5
Strawberry flavour	4	4	4	4

F9 is optimized formulation of Montelukast Sodium mouth dissolve tablets containing Indion 414. F10, F11 and F12 are different formulations tried with other superdisintegrants like Croscarmellose sodium, Sodium Starch Glycolate and Crospovidone.

TABLE 5: EVALUATION OF OPTIMIZED MOUTH DISSOLVE TABLETS FOR VARIOUS QUALITY CONTROL PARAMETERS

Parameter	F1	F5	F9
Appearance	Biconvex tablets offwhite in colour	Off white flat bevelled tablets	Off white flat beveled tablets
Texture	Smooth	Smooth	Smooth
Taste	Non bitter	Non bitter	Sweet
Dimensions	12 mm in diameter	9 mm in diameter	9 mm in diameter
Weight variation (mg) ± SD	460 ± 2.87	200 ± 2.15	150 ± 1.87
Hardness (kg/sq-cm)	3-4	3-4	3-4
In vitro dispersion time (s)	15	20	20
Drug content (%) ± RSD	100.12 ± 1.46	101.09 ± 1.28	99.18 ± 1.28
Drug release% (30 min)	87.26	92.89	95.49

Optimized formulations F1 (mouth dissolve tablets of roxithromycin), F5 (mouth dissolve tablets of Dicyclomine hydrochloride) and F9 (mouth dissolve tablets of Montelukast sodium) were evaluated for various quality control parameters.

TABLE 6: COMPARATIVE EVALUATION OF *IN VITRO* DISPERSION TIME OF MOUTH DISSOLVE TABLETS CONTAINING VARIOUS SUPERDISINTEGRANTS

Superdisintegrants	Roxithromycin mouth dissolve tablets	Dicyclomine Hydrochloride mouth dissolve tablets	Montelukast sodium mouth dissolve tablets
Indion 414 (Ion Echnage India Ltd)	15s	20s	20s
Sodim Starch Glycolate (Primojel)	20s	100s	15s
Crospovidone (Polyplasdone XL)	15s	35s	10s
Croscarmellose sodium (Ac-Di-Sol)	25s	30s	15s

transferred to a 100 ml measuring cylinder. Simulated saliva was added up to 25 ml. The measuring cylinder was shaken intermittently for the first 1 h and then kept aside for next 3 h. Volume occupied by the material at the end of 4 h was measured. Swelling index was calculated by the formula: (final volume-initial volume/ initial volume)×100. Complete taste masking of bitter drugs like roxithromycin and dicyclomine hydrochloride was achieved using 1:5 and 1:3 ratio of Indion 204 and Indion 204 (O) respectively. The mouth dissolve tablets were non-bitter with a good mouth feel. F1, F5 and F9 exhibited good dispersion time as compared to others. The results of comparison of *in vitro* dispersion time of Indion 414 with croscarmellose sodium, sodium starch glycolate and crospovidone are shown in Table 6. The formulations F4, F8 and F12, showed pitted surface, whereas F1, F5 and F9 appeared smooth. The hardness of the formulations was 3-4 kg/sq cm. Drug content of the formulations was within limits with more than 80% of drug release in 30 min. Swelling index of the superdisintegrants is given in Table 7, with Indion 414 showing good swelling.

TABLE 7: COMPARATIVE EVALUATION OF SWELLING VOLUMES OF VARIOUS SUPERDISINTEGRANTS IN SIMULATED SALIVA

Superdisintegrant	Initial Volume	Final Volume	Swelling power
Indion 414	1ml	9ml	800
Sodim Starch Glycolate	1ml	17ml	750
Crospovidone	5ml	5ml	20
Croscarmellose sodium	2ml	16 ml	700

Thus, Indion 414 exhibited very good superdisintegrant action resulting in a cost-effective formulation. Their use can be extended to various other fast disintegrating dosage forms.

ACKNOWLEDGEMENTS

This work has been sponsored by Ion Exchange (India) Ltd, Mumbai and was presented at the fifth International Symposium on Advances in Technology and Business Potential of New Drug Delivery Systems organized by Controlled Release Society (Indian Chapter) 2004, Mumbai.

REFERENCES

1. Sastry, S.V., Nyshadham, J.R., and Joseph, A.F., **Pharm. Sci. Tech. Today,** 2000, 3, 138.
2. Shangraw, R., Mitrevej, A. and Shah M., **Pharma Tech**., 1980, 4, 49.
3. Caramella, C., **Drug Develop. Ind. Pharm**., 1990, 26, 2561.
4. Chang R.K., Guo, X., Burnside, B.A., and Couch, R.A., **Pharma Tech**., 2000, 24, 52.
5. Nakamichi, K., Isumi, S., Yassura H., **European Patent** No 0627218,1994.
6. Mehendale, S.V. and Malshe, V.C., **Eastern Pharmacist,** 1991, 41.
7. Amin P.D., Wadhwani A.R. and Prabhu N.B., **Indian. J. Pharm. Sci**., 2004, 66, 670.

Accepted 25 February 2006
Revised 25 April 2005
Received 16 November 2004
Indian J. Pharm. Sci., 2006, 68 (1): 117-119