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DESIGNING OF ORODISPERSIBLE TABLET OF DIETHYL CARBAMAZINE CITRATE FOR THE TREATMENT OF FILARIASIS

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ABSTRACT: The main aim of the study was to develop orodispersible tablets of diethyl carbamazine citrate (an anthelmintic) for improving patient compliance,especially those of paediatric & geriatric categories with difficulties in swallowing. In the wet granulation method mixture of sodium bicarbonate and tartaric acid along with agar were used as disintegrants. The tablet formulation containing 28 mg of agar, 26 mg of sodium bicarbonate and 26 mg of tartaric acid considered as the overall best formulation (with an in vitro dispersion time of approx. 54.39 sec and in vitro drug release of 98.4 %) Short term stability studies (at 40±2ºC/75±5% RH) on the best formulation indicated that there no significant changes in drug content. IR spectroscopic study indicated that there are no drug excipient interactions. The use of mixture of tartaric acid and sodium bicarbonate further assists in taste masking. Undoubtedly the availability of various technologies and the manifold advantages of orodispersible tablets will surely enhance the patient compliance providing rapid onset of action.

Keywords: Diethyl carbamazine citrate, Orodispersible tablets, IR spectroscopy

INTRODUCTION

Recent advances in novel drug delivery systems (S Bhaskran, et al., 2002) aim for designing dosage forms, convenient to be manufactured and administered free side effects, offering immediate release and enhance bioavailability so as to achieve better patient compliance. Though oral drug delivery systems (Y W Chein et al., 1992), preferably tablets are most widely accepted dosage forms for being compact offering uniform dose and painless delivery. But disphagia is a common problem for all age groups especially the elderly and paediatrics, because physiological changes associated with those groups(R Chang, et al., 2000 and B S kuchekar, et al., 2005). The disphagia is seen nearly 35% of general population and associated with a number of conditions like parkinosonism, mental disabilities, motion sickness, unconsciousness, unavailability of water etc.. To overcome such problems certain innovative drug delivery system like mouth dissolving tablets have been developed. These are novel dosage forms which dissolve in saliva within few seconds when put on tounge. The orlly disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, fast disintegrating tablets, porous tablets, rapimelts (S Lindgreen, et al., 1993 and Y S Bhushan, et al., 2000).The mouth dissolving tablets are absorbed from the mouth, pharynx and oesophagus as saliva pases down into the stomach. In these cases the bioavailability of drugs are significantly greater than those observed from conventional solid dosage forms such as tablets and capsules (G C Wilson, et al., 1987). In the present study orodispersible tablets of diethyl carbamazine citrate an antihelmintic(S C Sweetman, et al., 2002) were designed using wet granulation method using various excipients with prime objective arriving of a cost effective product.

MATERIALS AND METHODS

Diethyl carbamazine citrate was received as a gift sample from vecco labs pharmaceutical Ltd., Medchal, A.P, peppermint flavor and aspartame were obtained as gifts from aurobindo labs pvt Ltd, A.P. Sodium bicarbonate, Tartaric acid, Purified Talc, Starch, D-manitol and potassium dihydrogen-o-phosphate were procured from SD fine chem. Ltd Mumbai. Sodium hydroxide, sodium lauryl sulphate and methanol were procured from Qualigens fine chemicals Mumbai.

PREPARATION OF ORODISPERSIBLE TABLETS

Accurately weighed quantities of ingredients mentioned in Table-I were passed through sieve no. 60. And lubricant and glidant passed through sieve no.80. All the ingredients except sodium lauryl sulphate (lubricant) and Talc (glidant) were manually blended homogenous by way of geometric dilution. The mixture was moistened with aqueous solution and granulated with sieve no.60 and placed in hot air oven at 60º C for sufficient 3-4 hrs. Then dried granules passed through sieve no.60 and blended with sodium lauryl sulphate and talc. The homogenous mixture were placed into tablet punching machine getting tablet weight 190 mg each using deep concave punch having diameter of 8 mm. (10 station rotary tablet machine Clint India)

TABLE-I COMPOSITION OF ORODISPERSIBLE TABLET

Ingredients(mg)	ORD1	ORD2	ORD3	ORD4	ORD5	ORD6	ORD7
DEC	50	50	50	50	50	50	50
STARCH	40	36	34	32	28	26	20
MANNITOL	40	36	34	32	28	26	20
SOD.BICARBONATE	20	16	18	20	24	26	32
AGAR	12	28	28	28	28	28	28
TARTARIC ACID	20	16	18	20	24	26	32
ASPARTAME	2	2	2	2	2	2	2
SLS	2	2	2	2	2	2	2
PEPPERMINT	2	2	2	2	2	2	2
TALC	2	2	2	2	2	2	2
TOTAL WEIGHT	190	190	190	190	190	190	190

EVALUATION OF TABLET

Twenty tablets were selected at random and weighed individually. The individual weights were compared with the average weight for determination of weight variation. Hardness and friability of the tablets were determined by using Monsanto hardness tester and Roche friabilator respectively. For content uniformity test, ten tablets were weighed and powdered. The powder equivalent to 50 mg of drug was extracted in to methanol, filtered and the absorbance was measured at 255 nm after appropriate dilution. The drug content was calculated using the standard calibration curve. The mean percent drug content was determined as an average of three determinations. For determination of *in vitro* dispersion time, one tablet was placed in a beaker containing 10 ml of pH 6.8 phosphate buffers at 37±0.5º C and the time required for complete dispersion was determined. IR spectra of the drug and its formulations were obtained by potassium bromide pellet method using Perkin-Elmer FTIR series (model-1615) spectrophotometer in order to rule out drug-carrier interactions.

IN VITRO DISSOLUTION STUDY

In vitro dissolution of the orodispersible tablets was studied in USP XXIII type-II dissolution test apparatus (Electrolab, model: TDT-06N) employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer at 37+0.5ºC as dissolution medium.

One tablet was used in each test. Aliquots of dissolution medium were withdrawn at specified intervals of time and analyzed for drug content by measuring the absorbance at 255 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Percent of the drug released was calculated and plotted against time.

RESULTS AND DISCUSSION

All the compressible excipient by wet granulation method was prepared using starch along with mannitol. This excipient was evaluated for bulk density, tapped density and Carr's index.

Orodispersible tablets of DEC were prepared by using the above excipient and evaluated for pre-compression parameters such as bulk density, tapped density, Carr's index and angle of repose (Table II) and for post compression parameters such as hardness, weight variation, drug content uniformity and *in vitro* dispersion time (Table III).

TABLE II Pre-compression parameters of DEC formulations

Formulation code	Bulk density (gm/cc)	Tapped density (gm/cc)	Angle of repose (degree)	Carr's index (%)
ORD1	0.54	0.64	26.21	15.62
ORD2	0.53	0.61	25.74	13.11
ORD3	0.50	0.58	24.02	13.79
ORD4	0.49	0.56	25.51	12.50
ORD5	0.48	0.55	23.54	12.72
ORD6	0.47	0.54	22.68	12.96
ORD7	0.46	0.53	21.82	13.20

The bulk density of pre-compression blends was found to be in the range of 0.46 to 0.54 gm/cc, tapped density in the range of 0.53 to 0.64 gm/cc, the Carr's index values were in the range of 12.50 to 15.62% and angle of repose in the range of 21.82 to 26.21. The hardness of the tablet formulations was found to be in the range of 2.65 to 2.97 kg/cm^2. The friability values were found to be in the range of 0.70 to 1.01%. The weight of all the tablets was found to be uniform with low values of standard deviation and within the prescribed IP limits. The percent drug content of all the tablets was found to be in the range of 98.33 to 101.57% of the expected DEC content, which was within the acceptable limits. The results are shown in Table III.

TABLE III Post-compression parameters of DEC orodispersible tablet

Formulation code	Hardness(kg/cm^2)	Friability (%)	In-vitro dispersion time (sec)	% of drug content	Weight variation
ORD1	2.65	1.01	171.66	98.33	181-198 Within the I.P limits (±7.5%)
ORD2	2.68	0.98	91.41	98.67	
ORD3	2.75	0.92	78.55	98.52	
ORD4	2.79	0.81	66.26	98.21	
ORD5	2.81	0.79	61.29	100.23	
ORD6	2.77	0.70	54.39	99.54	
ORD7	2.97	0.73	58.79	101.57	

Among the tablets prepared formulation ORD6 containing 28 mg of agar, 26 mg of sodium bicarbonate and 26 mg of tartaric acid was found to be promising and has shown an *in vitro* dispersion time of 54.39 s (Fig. I).

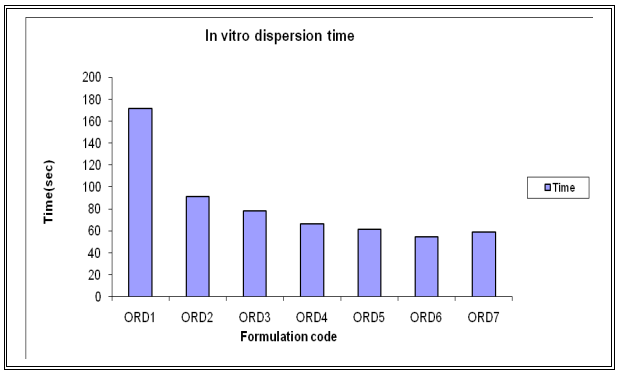

Fig. I: In vitro dispersion time of orodispersible tablets.

IN VITRO DRUG RELEASE STUDY

In vitro drug release studies were performed in pH 6.8 phosphate buffer, on the above promising formulation (ORD6) gives maximum amount of drug release comparing to other formulations. The Percentage of drug release of ORD6 is best giving 98.4%. The dissolution profiles of the above formulations are depicted in figure II.

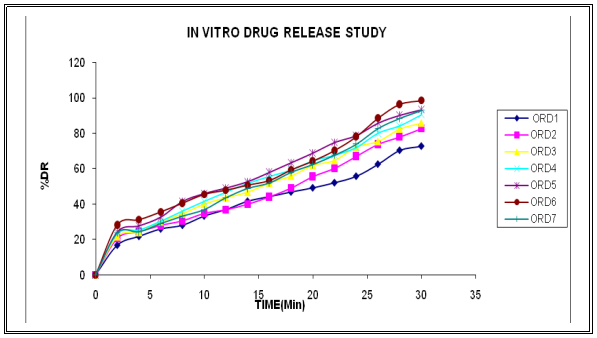

Fig. II: Comparative drug release study vs time plots.

SHORT-TERM STABILITY STUDIES

Short-term stability studies on the above promising formulation (at 40±2° / 75±5% RH for 3 months) have shown no significant changes in physical appearance, drug content and *in vitro* dispersion time. Statistical analysis ('t'-test) of drug content data gives 't' value of 2.17 for ORD6 formulation which is much less compared to the table value of 4.3 ($p<0.05$). There are no appreciable changes in *in vitro* dispersion time up on storage at 40±2° / 75±5% RH for 3 months period. The IR spectrum of the pure drug diethylcarbamazine citrate exhibits characteristic peaks at 3053, 1623, 1408 and 1266 cm-1 due to -CH stretching, -C=O stretching, -C-C stretching and CN aromatic stretching respectively. All the above characteristic peaks were found in the IR spectrum of the formulation ORD6. The presence of above peaks confirms undisturbed structure of drug in the above formulation. Hence, there are no drug-excipient interactions.

CONCLUSION

The study clearly demonstrates that orodispersible tablets of diethyl carbamazine citrates could be successfully prepared by direct compression method in a cost effective manner employing agar. The use of mixture tartaric acid and sodium Bicarbonate further assists in taste masking. Undoubtedly the availability of various technologies and the manifold advantages of orodispersible tablets will surely enhance the patient compliance providing rapid onset of action.

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