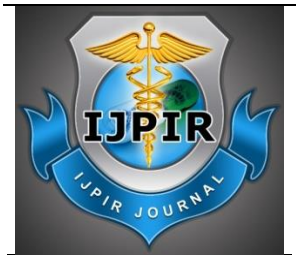
Research Article



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Formulation and evaluation of orodispersible tablets of cetirizine hydrochloride

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ABSTRACT

The main objective of this work is to formulate and evaluate Cetirizine HCl (OFDDS) using different concentrations of super-disintegrates like crosscarmellose sodium(CCS),sodium starch glycolate (SSG) and their combinations in different ratios. The in vitro disintegration time of Cetirizine HCl prepared by direct compression method by super disintegrates were found to be in the range of 18 to 11sec fulfilling the official requirements. The bulk density and tapped bulk density for the entire formulation blend varied from 0.506 gm/cc to 0.5342gm/ccand0.5831to0.6308respectively.Thefriabilitywasfoundinalldesignedformulations in the range 0.43 to 0.72% to be well within the approved range (<1%). The weight variation was found in all designed formulation in the range 96 to101 mg. The wetting time were found to be in the range of 11 to 18sec. Water absorption ratio for all the formulations found in the range 11 to 16%.combination of sodium starch glycolate and crosscarmellose sodium(6%of25%-ssg&75%ccs))promotes dissolution rate of drug release when compared to formulation of SSG & CCS alone. It may be due to capillary and wicking mechanism of SSG &CCS

Keywords: Orodispersible Cetirizine HCl Tablet, Crosscarmellose sodium, Sodium starch glycolate,

INTRODUCTION [1,2,3]

Drug delivery systems (DDS) have made a significant contribution to global pharmaceutical sales through market segmentation, and are moving rapidly. Orally disintegrating tablets (ODT) or "Mouth dissolving tablets", "Orodispersible tablets", "Melt-are oral solid dosage forms that disintegrate in the oral cavity in easy swallow residue. Recently as per United States Pharmacopoeia, British Pharmacopoeia, and Centre for Drug Evaluation and Research (CDER). US FDA, European pharmacopoeia defined ODT tablets as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue". ODT are easy to administer and lead to better patient compliance especially in elderly and children. The newest generation of ODTs can produce more robust ,versatile tablets that over come some of the limitations of earlier ODTs. Significantly broadening the applications of this dosage form. A key reason that companies choose an ODT over other delivery technologies is that it is a relatively easy and often less risky delivery option to develop. Since the route of administration remains the same, ODTs that are formulated as bioequivalent line extensions or generic versions of an existing oral dosage form have minimal clinical requirements to gain approval. There are several advantages Of Orally Disintegrating are: Ease administration for patients who are mentally ill, disabled and uncooperative, Can be designed to leave minimal or no residue in mouth after administration and also to provide a pleasant mouth feel. Improved stability, low sensitivity to environmental condition, Suitable for controlled/sustained release actives, Allows high drug loading, ability to provide advantages of liquid medication in the form of solid preparation, the new proprietary method allows the incorporation of microencapsulated drugs for enhanced bioavailability, flexibility of dosing & immediate and/or controlled release and superior therapeutic benefit.

DRUG PROFIL: Cetirizine Hydrochloride

ChemicalName:[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]acetic acid. Molecular formula: c21H26Cl2N2O3, Molecular Weight: 388.89, Description: Crystalline solid Melting point: 110-115 cCetirizine hydrochloride (CTZ) is an orally active and selective H1-receptorant agonist used in seasonal allergicrhinitis, perennial allergicrhinitis and chronicurticaria. CTZ is a white,

crystalline water soluble drug possessing bitter taste properties. Due to sore throat conditions, the patient experiences difficulty in swallowing a tablet type of dosage form. Thus, mouth fast dissolving tablets would serve as an ideal dosage form for the patients as well as pediatric patients who find it difficult to swallow the tablet.

Excipients Profile: Sodium starch glycolate (sodium carboxy methyl starch)

It is Tablet and capsule disintegrates**.** It is a Very fine, white or off white, free flowing powder; odorless or almost odorless. Practically insoluble in water, insoluble in most organic solvents It consists of oval or spherical granules, 30-100µm in diameter with some less-spherical granules ranging from 10-35 µm in diameter .Solubility: Insoluble in cold water, hot water. Stability: The product is stable. Storage:Keep container tightly closed .Keep container in a cool, well-ventilated area. Incompatible with ascorbicacid.

Applications

Sodium starch glycolate is widely used in oral pharmaceutical as a disintegrant in capsule and tablet formulations. It is recommended to use in tablet prepared by either direct-compressionor wet-granulation processes. The recommended concentration in a formulation is 2-8%, with the optimum concentration about 4% although in many cases 2% is sufficient.

Crosscarmellose Sodium

Croscarmellosesodiumisacrosslinkedpolymerofcarboxymeth ylcellulosesodium. Cross linking makes it an insoluble, hydrophilic, highly absorbent material, resulting in excellent swelling properties and its unique fibrous nature gives it excellent water wicking capabilities. Croscarmellose sodium provides superior drug dissolution and disintegration characteristics, thus improving bioavailability of formulations.

Application

Croscarmel lose sodium is used in oral pharmaceutical formulations as a disintegrants for capsules, tablets and granules. When used in wet granulations the croscarmellose sodium is best added in both the wetand dry stages of the process (intra- and extra granularly) so that wicking and swelling ability of the disintegrantis best utilized. Concentration of up to 5% w/w of croscarmellose sodium may be used as a tablet disintegrant although normally 2% w/w is used in tablets prepared by direct compression and 3%w/w in tablets prepared by a wet-granulation process

Magnesium stearate

Magnesium stearate is a fine, white, precipitated or milled, impalpable powder of low bulk density, having a faint odor of stearic acid and a characteristic taste. The powder is greasy to the touch and readily adheres to the skin.

Colloidal silicon di-oxide

Colloidal silicon dioxide is widely used in pharmaceutical, cosmetics, and food products. Its small particle size and large specific surface area give it desirable flow characteristics that are exploited to improve the flow properties of powder in a number of processes such as tableting. Colloidal Silicon dioxide is also used to stabilize emulsion and as athixo tropic thickening and suspend in gagent in gels and semi solid preparations.

Lactose mono hydrate

Lactose is milk sugar. It is a disaccharide composed of one galactose and one glucose molecule. In pharmaceutical industry, lactose is used to help form tablets because it has excellent compressibility properties. It is also used to form a diluents powder for dry powder inhalations.

MATERIALSANDMETHODS

Sl.No.	Materials	Source
1	Cetrizinehydrochloride	AurobindoPharma
2	Sodiumstarchglycolate	NihaltradersHyderabad
3	Croscarmelloussodium	NihaltradersHyderabad
4	Magnesiumstearate	SpanPharmaPrivateLimited Hyderabad,India.
5	Colloidalsilicondi-oxide	SpanPharmaPrivateLimited Hyderabad,India**.**
6	Lactosemonohydrate	SpanPharmaPrivateLimited Hyderabad,India**.**

Instruments and Equipments Used

Sl.No.	Instruments	Manufacturer/supplier
1	UVVisible spectrophotometer	Shimadzu1800
2	Multi station rotary punch tablet Compression machine	Clitpilotpresschamnnda
3	Dissolutiontestapparatus	Electrolab,USPTDT06P
4	FriabilityTester	Electrolab,USP EF
5	HardnessTester	Monsantohardnesstester
6	Tabletdisintegrationtester	Electrolab
7	Verniercalliper	Pico.indiaLtd

RESULTS&DISCUSSION

Pre-compression parameters

Powder ready for compression containing drug and various excipients were subjected for pre-compression parameters to study the flow properties of granules, to achieve uniformity of tablet weight. The results of all the preformulations parameters are given table

Angle of repose(θ):The data obtained from angle of repose for all the formulations were found to be in the range of 24.19° and 28.56° which reveals good flow property. All formulations showing angle of repose within 30°, indicates a good flow property of the granules.

Bulk density

Bulk density (BD) and tapped density (TD) for the blend was performed. The loose bulk density and tapped bulk density for the entire formulation blend varied from 0.508 gm/ccto0.5438 gm/cc and 0.5941 to 0.6408 respectively. Carr's compressibility index: The results of Carr's consolidation index or compressibility index (%) for the entire formulation blend ranged from 14.30% to 17.53% had shown excellent compressibility index values up to 15% result in good to excellent flow properties. As shown in previous research work.

Hardness

The hardness of all the tablets was maintained within the 2.00 kg/cm to 4.00 kg/cm. The mean hardness test results are tabulated in table.

Friability test

The friability was found in all designed formulations in the range 0.42 to 0.74% to be well within the approved range(<1%).The friability study results were tabulated in table.

Weight variation test

The weight variation was found in all designed formulation in the range 97 to 102 mg. The mean weight variation test results are tabulated in table. All the tablets passed weight variation test as the average percentage weight variation was within 7.5% i.e. in the pharmacopieal limits.

In-vitro disintegration time

Theinvitrodisintegrationtimeismeasuredbythetimetakentoundergouniformdisintegration.Rapiddisintegrationwithinseveral minuteswasobservedinalltheformulations.Theinvitrodisintegrationtimeof CetrizineHclpreparedbydirectcompression method by super disintegrates were found to be in the range of 18 to 11secfulfillingthe official requirements .Based on the in vitro disintegration time, formulation F12and F15 were found to be promising and showed a disintegration time of 18and 11 sec respectively. Disintegrating study showed that the disintegrating times of the tablets decreased withcombinationofbothsodiumstarchglycolateandcrosscarmellosewithdifferentconcentrations. It also showed least disintegration time in comparison with the all other formulation because of their lowest hardness and the porous structure is responsible for faster water uptake, hence it facilitates swelling action in bringing about fast disintegration.

Wetting time

Wetting time closely related to the inner structure of the tablet. The results of wetting time are shown in table. The wetting time were found to bein the rangeof11to 18sec.Water absorption ratio: Water absorption ratio for all the formulations found in therange11to 16%. The results of water absorption ratio for tablets were shown in table.

Table 1: Post-compression parameters of CetirizineHCl tablets

Formulation	Hardness	Friability	Thickness	Weight variation
F1	3.5	0.69	3.21	100
F2	3.5	0.46	3.30	99
F3	4.0	0.72	3.12	101
F4	4.0	0.72	3.29	102
F5	3.6	0.68	3.34	99
F6	3..5	0.43	3.36	98
F7	4.0	0.42	3.29	99
F8	3.8	0.45	3.36	97
F9	3.7	0.54	3.30	100
F10	3.9	0.57	3.21	98
F11	3.8	0.53	3.33	100
F12	3.7	0.41	3.12	101
F13	3.5	0.52	3.42	99
F14	3.3	0.40	3.32	100
F15	3.2	0.37	3.21	102

Post formulation studies

Table 2: Post formulation studies of Cetirizine HCL Tablets

Formulation code	In-vitro dispersion time(sec)	Wetting time(sec)	Water absorption (%)
F1	32	27	13
F2	28	25	17
F3	26	18	18
F4	50	33	13
F5	40	25	16
F6	30	21	15
F7	30	29	14
F8	26	26	14
F9	20	20	13
F10	26	26	14
F11	24	24	13
F12	18	23	12
F13	23	20	13
F14	19	15	12
F15	11	11	11

Dissolution

In vitro dissolution studies: Dissolution rate was studied by using USP type-2 apparatus using 900ml of phosphate buffer pH (6.8) as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5ºc, aliquot of dissolution medium withdrawn at every 15 sec interval and filtered. The absorbance of the filtered solution was measured by UV spectrophotometric method at 231nm and concentration of the drug was determined from the standard calibration curve. The dissolution of Cetirizine hydrochloride from the tablets is shown in the fig (table: 3) cumulative percentage drug release profiles. Cumulative percentage drug release profiles.

Table 3: In vitro dissolution studies of cetirizine HCl Tablets

Time(sec)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
15	32.7	40.7	41.7	34.3	35.5	36.3	33.5	31.4	36	32.0	33.7	30	33.4	36.6	47.6
30	36.8	43.3	43.7	38.8	39.7	43	34.7	38.7	40.8	36.0	38.5	38.7	36.6	44.3	561.4
45	43.1	47.8	48.1	4.19	44.4	49.7	36	42.3	44.7	38.8	40.4	44.4	41.8	51.4	64.8
60	56.6	57.4	58.4	44	50.1	59.4	40.4	48.2	58.8	42	45	60.6	42.5	54.7	70.6
75	61	65.8	68.8	50	57	67.6	44.7	55.7	62.8	46.4	53.5	66.3	48.3	53.9	75.7
90	65.9	66.4	69.3	60.7	62.5	70.9	49	65.5	67.7	51.5	67	70.2	51.9	66.5	81
105	69.7	71	72.7	66	73	74.3	56.3	65.9	69.4	59.4	73.4	74.5	57.7	71.6	89.4
120	73.1	74.5	75.6	79	80.4	81	79.5	79.6	80.0	76	78.7	81	77	83.9	96.7

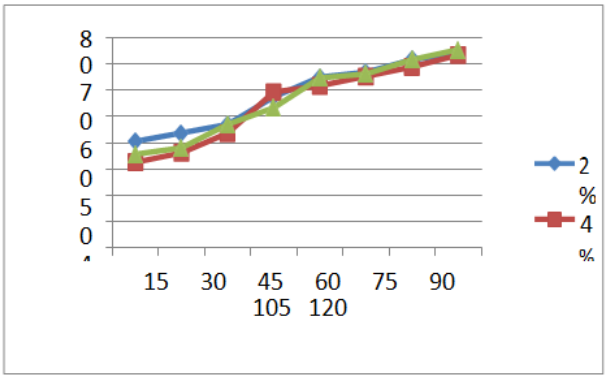

Fig1:Releaseprofileof formulation(F1,F2,F3)

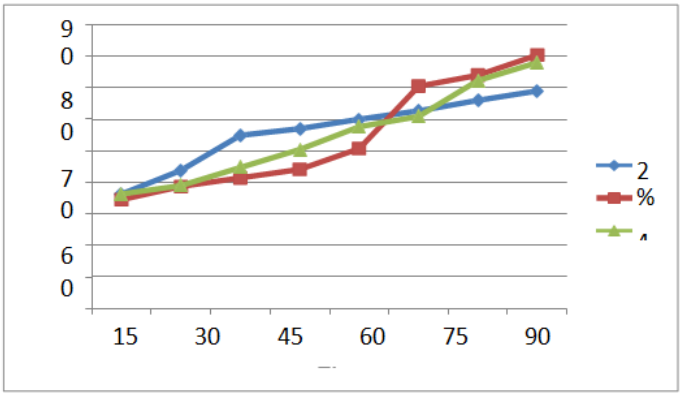

Fig2:Releaseprofileof formulationF4,F5,F6

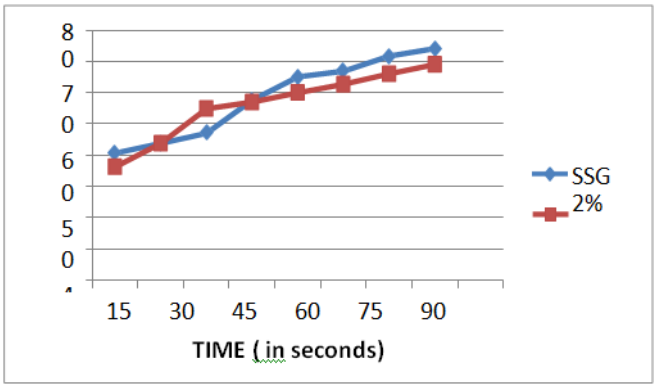

Fig3:Releaseprofileof formulationsF1, F4

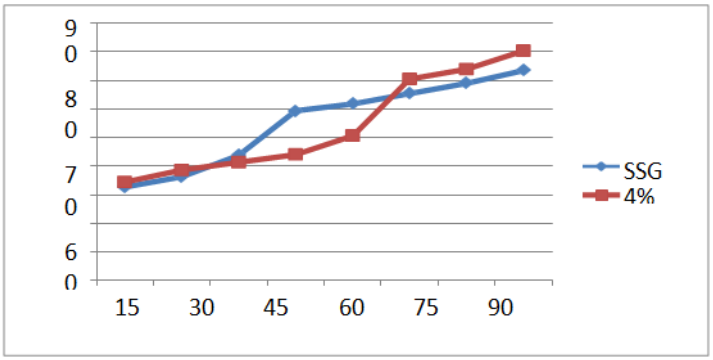

Fig4:Releaseof formulationsF2, F5

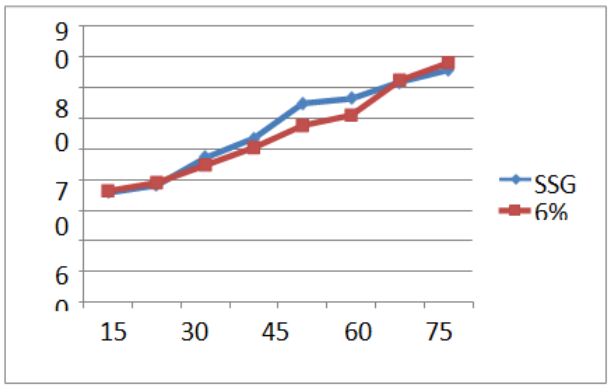

Fig5:Releaseprofileof formulationsF3, F6

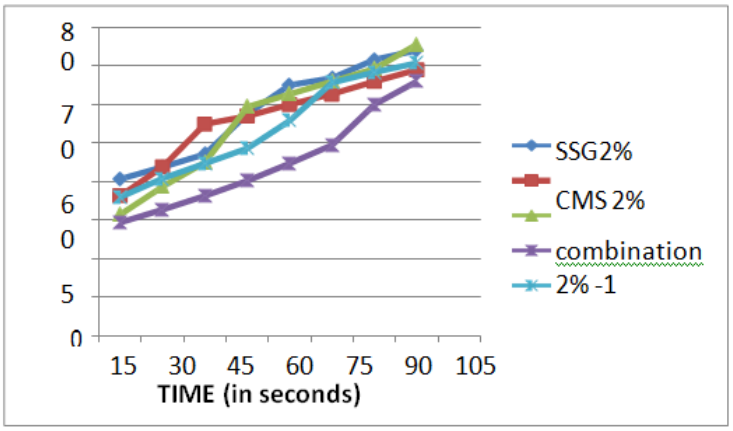

Fig6:Releaseof formulationsF1,F4, F7,F10, F13

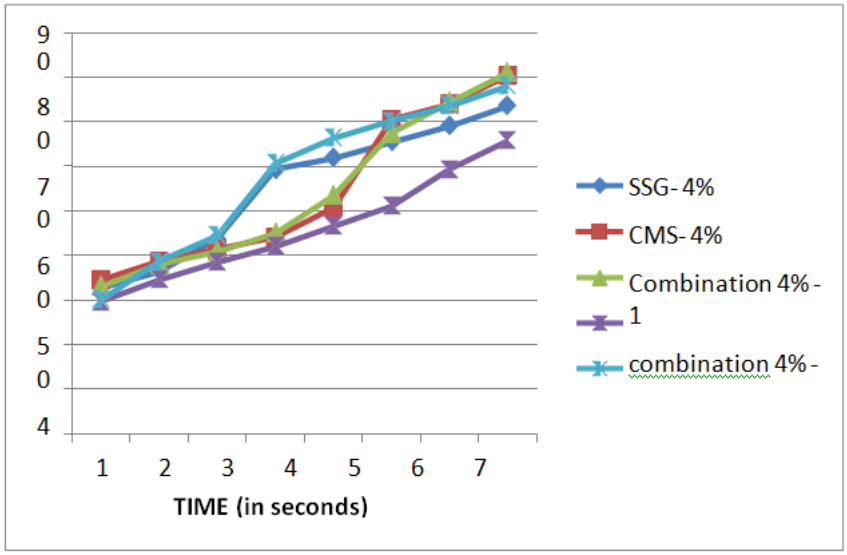

Fig 7:ReleaseofformulationsF2, F5, F8,F11, F14

CONCLUSION

In the present work fast dissolving tablets of Cetirizine hydrochloride By using super disintegrates were prepared by direct compression methods. The study demonstrate that effect of two different super disintegrates combination blend that is sodium starch glycolate (SSG) and crosscarmellose sodium (CCS)added in different ratios to a model formulation of cetirizine in order to compare dissolution performance of formulation with the formulation containing sodium starch glycolate (SSG) & crosscarmellose sodium (CCS) alone as disintegrates.CetirizineHCL10mgi.e.tabletwtof100mgprepar edusingdifferentconcentration of SSG & CCS alone as well as in combination at different ratio of 25:75,50:50 , 75:25.The dissolution profile of formulation made with combination of disintegrant 2%, 4%, 6% level were found to be in the order of (ssg:ccs) 25:75>50:50>75:25. All the tablets of Cetirizine hydrochloride were subjected to weight variation, hardness, friability, in vitro dispersion , drug content uniformity, water absorption ratio, wetting time, and invitro drug release. Base

don the above studies following conclusions can be drawn. Tablets were found to be good and were free from chipping and capping. Based on the invitro disintegration time, formulations 6% of (50:50ssg:ccs) & 6%(25:75 ssg:ccs) were found to be promising and showed a dispersion time ofwettingtimeof18secand11secrespectively,whichfacilitateth efasterdispersion.The drug release from fast dissolving tablets of Cetirizine hydrochloride were found to be in the rangeof90.0%to 96.29%.Among all the 15 formulations the best formulation is with 6% of(50:50 ssg:ccs combination) &6%(25:75 ssg:ccs combination)showed faster disintegration time within (18&11sec) when compared to the other formulations and it showed 96.0% drug release at the end of2 mins. From the above results of the study it can be concluded that combination ofsodium starch glycolate and crosscarmellose sodium (6% of 25%-ssg&75%ccs) could be the alternative approach to increase the dissolution of tablets when compared to the formula with sodium starch glycolate and crosscarmellose alone as disintegrates.

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