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Research Article

FORMULATION AND EVALUATION OF TASTE MASKED ORAL DISINTEGRATING TABLETS OF LORATADINE

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ABSTRACT

The aim of the present research work was to mask the intensely bitter taste of Loratadine and to formulate an orally-disintegrating tablet (ODT)) of the taste-masked drug. Loratadine is an anti-histamine that reduces the effects of natural chemical histamine in body there by reduces sneezing, itching, watery eyes and running nose. In this present study, Eudragit L-100 as the taste masking agent and sodium starch glycolate and croscarmellose sodium as super disintegrants were used. Taste masked granules of Loratadine were prepared using different ratios of Loratadine and Eudragit L-100 (1:1,1:2,1:3) by wet granulation method and evaluated for precompression parameters. The optimum ratio (1:3) of drug and Eudragit L-100 was selected based on taste masking effect for preparing Oral disintegrating tablets of Loratadine using different percentages of the super disintegrants (3%, 6%, 9%) by wet granulation method. The prepared tablets were evaluated for post compression parameters like hardness, friability, disintegration time, *invitro* dissolution studies.From this study, it is concluded that the taste masked Loratadine oral disintegrating tablets can be successfully prepared by EudragitL-100 as a taste masking agent (1:3) and sodium starch glycolate (9%) as super disintegrant as it has shown 100% drug release with in 20 mins.

Keywords: Oral disintegrating tablets, Loratadine, Eudragit L-100, SSG, wet granulation method.

INTRODUCTION

For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of administration owing to its several advantages and high patient compliance compared to many other routes[1]. The oral route of administration is considered as the most widely accepted route because of its convenience of self administration, compactness and easy manufacturing[2,3]. Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. Orally disintegrating tablets(ODTS) are a new generation of formulations which combine the advantages of both liquid and conventional tablet formulations, and at the same time, offer added advantages over both the traditional dosage forms. . This may be defined as uncoated tablets intended to be placed in the mouth where they disperse readily within 3 min before swallowing[4]. When such tablets are placed in the oral cavity, saliva quickly penetrates into the pores to cause rapid tablet disintegration[5].Since ODTs rapidly disintegrate in saliva or in a small volume of water, elderly, infants, and dialysis patients with restricted water intake can easily ingest them. The ODT has remarkable disintegration properties as it can rapidly disintegrate without water in the mouth within few seconds. But, ODTs unlike conventional tablets, allow patients to taste the

drug, hence taste masking is must for ODT to avoid unpleasant or bitter taste of the drug which often leads to patient's non-compliance.
Several taste masking options are available, including sensory masking by adding correctives, chemical masking etc. The sensory masking method being simple and in-expensive is usually the first choice. Loratadine is a H1-receptor antagonist and has an intensely bitter taste. So the present research work was aimed at the successful masking of taste incorporate drug directly in to an ODT.

MATERIALS AND METHODS

Materials

Loaratadine and Eudragit L-100 were gift samples from Spectrum labs, Hyderabad. Sodium starch glycolate(SSG), croscarmellose sodium(CCS), mannitol, aspartame, magnesium stearate, talc were obtained from commercial sources. All the reagents were of analytical grade.

Preparation of taste masked granules[6]

Drug and Eudragit L-100 were mixed in different ratios(1:1, 1:2, 1:3) properly and the granules were prepared by means of the wet granulation method using starch paste as a binder. The granules were dried at 60° C for 24 hrs and the granules that passed through a 20-mesh sieve but remained on a 22-mesh sieve were used in this study.

Taste evaluation of granules[7-10]

A sensory test on taste of all granule preparations was performed using 6 healthy adult volunteers from whom informed consent was first obtained. They rinsed their mouthcavities sufficiently before and after tasting. The prepared granules were kept in the volunteers mouth for 30s and then spit out. The taste score was set to the range of 0-4 based on the degree of taste masking (0-Good,1-Taste less,2-Slightly bitter, 3-bitter ,4-very bitter.) Then based on scores, the best taste masked (1:3) granules were selected as optimized.

Preparation of Tablets

ODT tablets were prepared using super disintegrants by direct compression method. Different percentages of CCS and SSG were used(3,6,9 %). The composition used for preparation of ODT are given in the Table No 1. Accurately weighed optimised taste masked granules were mixed with croscarmellose sodium/sodium starch glycolate, Mannitol aspartame using blender for about 10-15 minutes. Then magnesium stearate and talc were added and mixed for further 10 minutes and compressed in to tablets by direct compression method using rotary type tablet punching machine(Cadmach)

Evaluation of Loratadine ODT'S

Pre compression parameters

The uniformly mixed powders of all formulations were evaluated for following parameters before compression.

a) **Angle of repose (θ)[11]** : The frictional forces in a loose powder can be measured by the angle of repose, θ. This is the maximum angle possible between the surface of a pile of powder and the horizontal plane. It is used to find the flow properties of powder and calculated using an equation1
Equation 1: Tan θ = tan-1 (h/r)
Where, θ is the angle of repose, H is the height in cm, R is the radius in cm.

b) **Bulk density (Db)[12] :** It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder into a measuring Cylinder and the volume was noted. It is expressed in gm/ml and is determined by an equation 2
Equation 2: Db=M/V0

c) **Tapped Density (DT):** It is the ratio of total mass of powder to the tapped volume of powder. The tapped volume was measured by tapping the powder to constant volume. It is expressed in gm/ml and is determined by an equation 3
Equation 3: DT=M/V1 Where, M is the mass of powder, V1 is the tapped volume of the powder.

d) **Carr's index/compressibility index:** Carr's Index is measured by using the values of the bulk density and tapped density by an equation 4
Equation 4: Carr's index= Tappeddensity-Poured density/Tapped densityx100

e) **Hausner's ratio:** Based on the tapped density and bulk density the hausner's ratio of the tablet blend was computed by an equation 5
Equation 5: Hausner's ratio (H) =Tapped density / Bulk density

Post compression Parameters

Then the tablets were evaluated for following parameters

a) **Thickness:** Thickness was determined for 20 pre weighed tablets of each batch using a vernier calipers scale and the average thickness was determined in mm.

b) **Hardness:** Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It was expressed in Kg/cm². Five tablets of each formulation were randomly picked and hardness of the each tablet was determined. Then the average hardness value was calculated.

c) **Friability[13]:** The friability of tablets was determined using Roche friabilator. It is expressed in percentage (%). 10 tablets were randomly selected and their initial weight was noted. Then tablets were transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes. The tablets were taken out the weight was noted again. For conventional tablets the percentage loss in friability should be less than 1% where as friability values of up to 4% are acceptable for oral disintegrating and chewable tablets.

d) **Weight variation test:** 20 tablets were selected randomly from a batch and were individually weighed and then the average weight was calculated. The tablets meet the USP specifications, when not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limits.

e) **Wetting time[14]:** Wetting time of dosage form is related with the contact angle. Wetting time of the mouth dissolving tablets is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. It can be measured using the following procedure. Procedure: Five circular tissue papers of 10cm diameter were placed in a Petri dish with 10cm diameter. 10ml of water was added to Petri dish, a tablet was carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet was noted as wetting time.

f) **Water absorption ratio(R) :** The weight of the tablet in the above procedure before keeping in to the Petri dish was noted (Wb). The wetted tablet from the Petri dish was taken and re weighed (Wa) using the same. The Water absorption ratio(R) was determined as per the equation 6. Equation 6: R=100(Wa-Wb)/Wb

g) ***In-vitro*** **disintegration time:** Disintegration time is the time taken by the tablet to break into smaller particles. The disintegration test is carried out using USP disintegration test apparatus containing a basket rack assembly with six glass tubes which consists of a 10 mesh sieve. The basket is raised and lowered 28-32 times per minute in the medium of 900ml of 0.1NHCl which is maintained at 37±2°C. Six tablets were placed in each of the tubes and the time required for complete passage of tablet fragments through the sieve (# 10) was considered as the disintegration time of the tablet. And the time for disintegration of FDTs were tabulated.

h) **Dissolution studies:** In vitro dissolution studies for all the fabricated tablets was carried out using USP paddle method at 100 rpm in 900 ml of phosphate buffer Ph 6.8 as dissolution media, maintained at 37 ± 0.5° C. 5 ml aliquot was withdrawn at specified time intervals, filtered through whattman filter paper and assayed spectrophotometrically at 247 nm. An equal volume of fresh medium, which was pre-warmed at 37°C , was replaced in to the dissolution media after each sampling to maintain the constant volume throughout the test.

RESULTS AND DISCUSSIONS

Taste evaluation was done using the time intensity method on 6 healthy human volunteers from whom informed consent was first obtained. Bitterness was recorded immediately and at several intervals for minutes according to the bitterness intensity scale from 0 to 4 where, 0-Good,1-Taste less,2-Slightly bitter, 3-bitter ,4-very bitter. Then based on scores, the best taste masked (1:3) granules were selected as optimized as shown in table no.2

The values for angle of repose were found to be within the range of 25°-30°. Bulk densities and tapped densities of various formulations were found to be within the range of 0.25 to 0.28(gm/cm²) and 0.30 to 0.35 (gm/cm²) respectively. Carr's index was found to be within the range of 13.0% to 20.0%. The Hausner s ratio was within the range of 1.10 to 1.25 as shown in table 3 from the result. It was concluded that the powder blends have good flow properties .which confirms the uniform filling during compression into tablets.

Hardness for all the formulations were in range of 3.5 to 4.10 kg/cm², it indicated that all the formulations possess sufficient mechanical strength .Weight variation was found to be within IP limits. Friability values were found to be less than 1% indicated that within the IP limits. Wetting time of all the formulations was found to be in the range of 26 to 43 seconds, and Water absorption ratio of all the formulations was found to be within the range of 95 to 115. Among all the formulations, FC formulation has shown least wetting time and highest water absorption ratio. In vitro disintegration time of all formulations was in the range of 20 to 38 seconds. Among all the formulations (FA-FF), FC containting 9% of sodium starch glycolate as super disintegrant showed rapid disintegration with low disintegration time of 20 seconds as shown in table no.4.

In vitro drug release studies shown in table 5. It revealed that drug release rate was increased with increasing concentration of superdisintegrants. Among all the formulations FC formulation in which sodium starch glycolate (9%) used as super disintegrant increased drug release rate compare to other superdisintegrants. Hence disintegration was rapid, thus it FC formulation has faster drug release than other formulations. Hence FC formulation was selected as best or optimized formulation. As 100% was released within 20minutes.

CONCLUSION

This study discusses the formulation and evaluation of taste masked oral disintegrating tablets of loratadine. From the above results and discussion, it was concluded that the ODT of Loratadine using 9% of sodium starch glycolate has shown 100% drug release with in 20 min. Hence the preparation of ODT of Loratadine with 9% of sodium starch glycolate was successful.

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Table 1: Composition of different formulations of taste masked ODT tablets

Mg						
Name of compound	**FA**	**FB**	**FC**	**FD**	**FE**	**FF**
Granules (containing Loratidine10mg)	40	40	40	40	40	40
Sodium starch Glycolate	6	12	18	-	-	-
Croscarmellose sodium	-	-	-	6	12	18
Mannitol	142	136	130	142	136	135
Aspartame	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5
Talc	5	5	5	5	5	5
Total (mg)	200	200	200	200	200	200

Table 2: Scores of taste masking

Ratio	Scores given by 6 volunteers						Total score
	1	**2**	**3**	**4**	**5**	**6**	
1:1	3	2	2	3	3	3	16
1:2	1	2	2	1	1	2	09
1:3	0	0	1	0	0	0	01

Table 3: Precompression parameters

S. No.	Parameters	Formulation Code					
		FA	FB	FC	FD	FE	FF
1	Bulk Density(g/ml)	0.26±0.02	0.28±0.01	0.28±0.03	0.27±0.01	0.25±0.02	0.27±0.021
2	Tapped Density(g/ml)	0.33±0.01	0.32±0.02	0.34±0.01	0.31±0.010	0.30±0.023	0.33±0.012
3	Angle of repose(θ)	25.3±0.1	24.12±0.3	26.71±0.2	27.41±0.1	28.36±0.3	28.91±0.4
4	Carr's Index (%)	19.6±0.3	13.58±0.2	15.52±0.1	13.14±0.2	18.21±0.2	19.45±0.1
5	Hausner's ratio	1.24±0.07	1.15±0.06	1.18±0.03	1.15±0.09	1.22±0.08	1.24±0.05

Table 4: Evaluation of the ODT tablet formulations

Formulation parameters	FA	FB	FC	FD	FE	FF
Weight (mg) (±SD)	199.5±1.21	200.3±1.11	200.2±1.28	200.8±1.31	199.6±1.07	199.6±1.02
Thickness (mm) (±SD)	3.74±0.008	3.82±0.003	3.79±0.014	3.77±0.011	3.79±0.016	3.80±0.014
Hardness (Kg/cm^2) (±SD)	4.09±0.29	4.05±0.32	4.07±0.34	4.0±0.12	3.9±0.23	4.03±0.11
Friability (%)	0.42	0.35	0.38	0.40	0.43	0.52
Disintegration time (sec) (±SD)	22±1	24±2	20±1	34±2	35±1	38±1
Wetting time (sec) (±SD)	26±2	28±1	32±2	35±1	42±1	41±2
Water Absorption ratio	98±3.2	104±3.8	113±1.5	89±1.42	96±1.74	111±3.2

Table 5: *In*vitro dissolution studies for FA-FF formulations

Time (min)	Sodium starch glycolate			Croscarmellose sodium		
	FA	FB	FC	FD	FE	FF
5	53.7±0.91	56.7±0.74	65.7±0.8	43.4±0.91	47.7±0.54	53.7±0.24
10	65.8±0.75	68.3±0.29	78.8±0.7	54.5±0.82	57.3±0.32	60.5±0.31
15	77.0±0.56	80.9±0.32	89.3±0.5	65.8±0.67	68.2±0.89	71.8±0.55
20	85.2±0.34	89.4±0.45	99.6±0.9	72.7±0.75	75.5±0.64	81.1±0.67
25	89.5±0.21	92.3±0.32	-------	79.5±0.42	82.3±0.59	87.5±0.35
30	94.1±0.90	96.5±0.89	--------	84.6±0.06	89.1±0.19	93.8±0.15

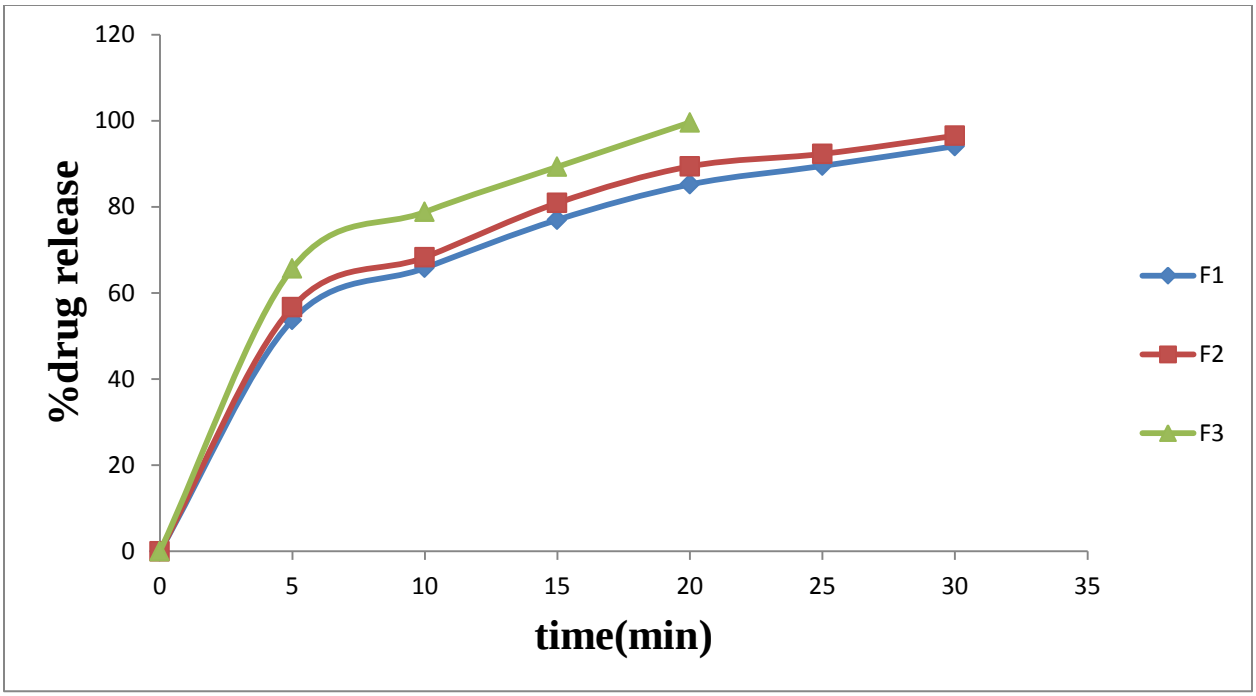

Fig. 1: Comparative *invitro* dissolution studies for F1, F2, F3 formulations

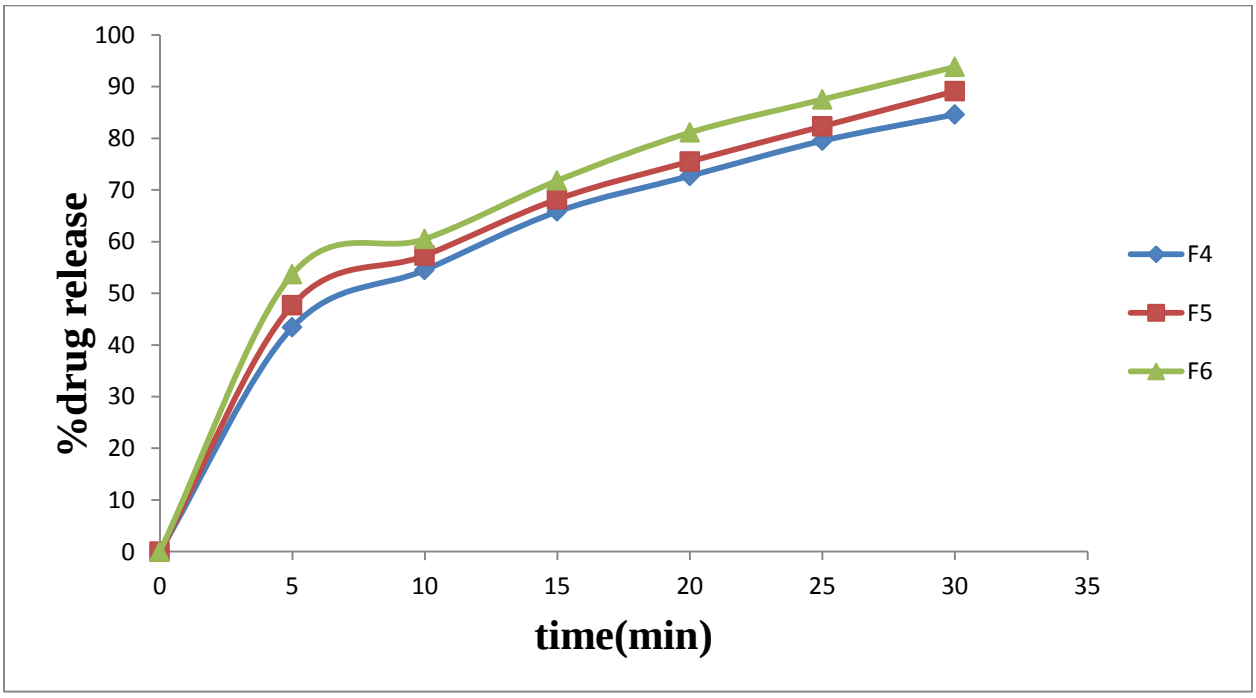

Fig. 2: Comparative *invitro* dissolution studies for F4,F5,F6 formulations

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