WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 14, 846-858. Research Article ISSN 2277–7105

FORMULATION AND EVALUATION OF SUGAR FREE SUCRALFATE CHEWABLE TABLETS

M. Rajesh*[1], Blessy Susan Varghese[1], Bency Susan Varghese[1], Shaik Shafi Quddin[2], P. Ramkumar[2]

[1]Department of Pharmaceutics, Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi, Tamil Nadu, India.

[2]Research and Development Department, Fourrts (India) Laboratories Pvt. Ltd, Kelambakkam, Chennai, Tamil Nadu, India.

Article Received on
11 Sep. 2017,
Revised on 01 October 2017,
Accepted on 22 October 2017
DOI: 10.20959/wjpr201714-9988

***Corresponding Author**
Dr. M. Rajesh
Professor & Head, Department of Pharmaceutics, Sankaralingam Bhuvaneswari College of Pharmacy, Sivakasi, Tamil Nadu, India.

ABSTRACT

Sucralfate is a cytoprotective drug for treating duodenal ulcer and gastric ulcer. The objective of the study was to develop an effective formulation of sugar free sucralfate chewable tablets thereby decreasing the drawbacks of commercially available suspensions and uncoated tablets of sucralfate and making the formulation suitable for both diabetic and non-diabetic patients. Sugar free sucralfate chewable tablets were prepared by wet granulation method using croscarmellose sodium and sodium starch glycolate as superdisintegrants and neotame as non calorific sweetener. The formulated tablets were evaluated for thickness, hardness, weight variation, friability, disintegration test, drug content, acid neutralizing capacity and *in-vitro* dissolution studies. The FT-IR spectral studies revealed that there was no interaction between the drug and excipients. Formulation SCT-7 showed rapid drug release (92.3%) at the end of 25 minutes and good acid neutralizing capacity (17.44 mEq) compared to other formulations. Hence the study concludes that formulation SCT-7 containing combination of two superdisintegrants (croscarmellose sodium and sodium starch glycolate) was found to be the better one which satisfied all the criteria for chewable tablets.

KEYWORDS: Chewable tablet, Croscarmellose sodium, Neotame, Sodium starch glycolate, Sucralfate.

INTRODUCTION

Chewable tablets are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing.[1] These tablets are intended to disintegrate smoothly in mouth at a moderate rate either with or without actual chewing.[2] Chewable tablets are often employed when the active ingredient is intended to act in a localized manner rather than systemically.[3]

Sucralfate is a locally acting substance that in an acidic environment (pH < 4) reacts with hydrochloric acid in the stomach to form a cross-linking, viscous, paste-like material capable of acting as an acid buffer for as long as 6 to 8 hours after a single dose.[4] The dose of Sucralfate uncoated tablet is 1G and hence, the size of the tablet is too large and difficult to swallow by the patients. If the dose of drug is reduced, more number of tablets needs to be administered for the maintenance of its therapeutic effect throughout the day. In case of Sucralfate suspension, the dose is 1000mg/10ml. Due to the high carbohydrate content of Sucralfate suspension, episodes of hyperglycemia have been reported in diabetic patients and it necessitates adjustment of the anti-diabetic treatment dose while using Sucralfate suspension. A total of seven formulations (SCT-1 to SCT-7) were prepared and the work was aimed to minimize the inherent drawbacks of commercially available suspensions and uncoated tablets of Sucralfate thereby improving the patient compliance, convenience in administration and therapeutic effectiveness of Sucralfate and making the formulation suitable for both diabetic and non-diabetic patients.

MATERIALS AND METHODS

Materials

Sucralfate was obtained from Zhejiang Haisen Pharmaceutical Co. Ltd, China. Mannitol was procured from Shandong Tunali Pharma, China. Neotame was procured from Nutra Sweet Company, Jaipur. Croscarmellose sodium was procured from Balanver Farmoquimica. Ltd, Brazil. Sodium starch glycolate was procured from DFE Pharma, Cuddalore, Tamilnadu. All other chemicals and reagents used were of analytical grade.

Methods

Preparation of Sucralfate Chewable Tablets

Chewable tablets containing 1000 mg of Sucralfate were prepared by wet granulation method. Sucralfate was sifted through #20 mesh, mannitol and starch were sifted using #40 mesh. Neotame was sifted through #100 mesh. Sodium starch glycolate and pregelatinized

starch were sifted through #60 mesh. The sifted powders are mixed in polythene bag for 5 minutes. The binder solution was prepared by dissolving gelatin in hot water under stirring condition. Add water containing starch and sunset yellow supra slowly with continuos stirring to it. Add specified quantity of preservatives and the solution was mixed for 2 minutes. The prepared binding solution was added slowly to the dry mixed powder and granulated using kneading method. The wet mass is dried at a temperature of 60^0C until the LOD (loss on drying) of granules is reached less than 5.5%. The dried granules were sifted through #20 mesh. The above dried granules are lubricated using croscarmellose sodium sifted through #60 mesh, starch, orange flavour and aerosil sifted through #40 mesh, magnesium stearate sifted through #60 mesh. The contents were mixed finally for 5 minutes in polythene bag. The final lubricated granules were compressed using rotary tablet compression machine of punch size 20 mm. The composition of Sucralfate chewable tablets are given in (Table 1).

Table 1: Composition of Sucralfate Chewable Tablets

SUCRALFATE CHEWABLE TABLETS								
S.No.	**Ingredients**	**Formulation Code (mg/tab)**						
		SCT-1	**SCT-2**	**SCT-3**	**SCT-4**	**SCT-5**	**SCT-6**	**SCT-7**
1	Sucralfate	1000	1000	1000	1000	1000	1000	1000
2	Mannitol	600.95	400	400	285	290	300	295
3	Starch	-	124	124	55	2.8	50	45
4	Neotame	-	5	5	3	6	3	3
5	Aspartame	17.5	-	-	-	-	-	-
6	CCS	-	-	-	30	30	-	-
7	SSG	10	12	12	-	-	10	15
8	Pregelatinized starch	62	44.25	44.25	18.25	15.45	40	40
9	Gelatin	-	-	-	-	-	64.7	64.7
10	MCC	-	-	-	34	20	-	-
11	Starch	-	-	-	-	50	78	80
12	Povidone K30	78	75	75	65	70	-	-
13	Methyl paraben	1	1	1	1	1	1	1
14	Propyl paraben	0.5	0.5	0.5	0.5	0.5	0.5	0.5
15	Purified water	qs	qs	qs	qs	qs	qs	qs
16	Sunset yellow (s)	0.05	0.25	0.25	0.25	0.25	0.3	0.3
17	CCS	-	28	28	25	25	30.5	40
18	Starch	-	-	-	18	12	20	20
19	Aerosil	-	-	-	-	10	-	3.5
20	HPC	-	-	30	-	-	-	-
21	Orange flavour	12	70	65	55	50	60	65
22	Magnesium stearate	18	15	15	10	17	17	17
Weight of each tablet (mg)		**1800**	**1775**	**1800**	**1600**	**1600**	**1675**	**1690**

PRECOMPRESSION PARAMETERS

Evaluation of Sucralfate Granules[5, 6, 7]

The prepared granules were evaluated for angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose of the granules was determined by fixed funnel method to assess the flow property. Bulk density is the ratio between a given mass of the powder or granules and its bulk volume. Tapped density is the ratio between a given mass of powder or granules and the constant or fixed volume of powder or granules after tapping. Bulk and tapped density were determined using digital bulk density apparatus. The compressibility index and the Hausner ratio are determined by measuring both the bulk volume and tapped volume of a powder or granules.

POSTCOMPRESSION PARAMETERS

Evaluation of Sucralfate Chewable Tablets

General Appearance and Thickness[8]

The general appearance of all tablets, its visual identity and overall elegance is essential for consumer acceptance. The formulated chewable tablets were evaluated for organoleptic characters such as, colour, odor and taste. The tablets were examined externally under a biconvex lens for surface cracks, depression and pinholes. The thickness of the tablets were measured by using digital Vernier caliper.

Hardness

Hardness is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength.[8] The hardness was measured using Monsanto Hardness tester. The values were expressed in Kg/cm^2.

Weight Variation Test

Twenty tablets of each formulation were selected at random and weighed individually. The weight of individual tablets was noted. Average weight was calculated and the individual weights were compared with the average weight.[8] The weight of not more than two tablets must not deviate from the average weight by more than±5%.

Friability Test

The friability of tablets was determined by using Roche Friabilator. Ten tablets were weighed and placed in friabilator and rotated at 25 rpm for 4 minutes.[8] Then the tablets were taken

out, dedusted and reweighed. The percentage friability of the tablets were calculated by the following equation.

Percentage Friability = [(Initial Weight – Final Weight)/ Initial Weight] × 100.

Disintegration Time[9]

Disintegration of sucralfate chewable tablets was carried out by using Disintegration test apparatus. The test was carried out on six tablets at $37^0C \pm 2^0C$ using distilled water as disintegration medium and the time in seconds taken for complete disintegration of the tablets with no palpable mass remaining in the apparatus was measured in seconds.

Acid – Neutralizing Capacity (ANC)[10]

Weigh accurately about 421.75 mg of powdered tablet into 250ml glass stoppered conical flask and add 100 ml of 0.1N hydrochloric acid previously heated to 37^0C. Cap the bottle, place it in a 37^0C water bath and stir the contents continuously for 1 hour. Cool to room temperature and transfer 20 ml of contents to a 100ml beaker. Add 30ml of water and titrate with 0.1 N Sodium hydroxide solution. Perform a blank titration on a mixture of water and 0.1N hydrochloric acid (30:20). Calculate the acid neutralizing capacity using the following expression.

$$\text{ANC} = \frac{5N\ \text{Titre value(Blank}-\text{sample)} \times \text{Average weight of tablet in mg}}{\text{Sample weight in mg}}$$

Drug Content Estimation by HPLC Method[11]

Preparation of mobile phase

Dissolve 132 gm of Ammonium sulfate in 900ml of water, dilute with water to 1000ml and mix. Adjust with phosphoric acid to a pH of 3.5±0.1, filter and degas.

Preparation of standard solution

Weigh accurately about 50 mg of potassium sucrose octasulfate reference standard in dried stoppered flask and add 5ml of mobile phase. Sonicate for 5 minutes and dissolve well.

Preparation of sample solution

Weigh accurately about 760 mg of powdered tablets in a centrifuge tube and shake at a moderate rate on a vortex mixture. Add 10 ml of a mixture of 4 N sulphuric acid and 2.2 N sodium hydroxide(1:1). Sonicate with swirling for 5 minutes, keeping the temperature of the mixture below 30°C. Immediately transfer the tube to vortex mixer and add 0.1M sodium hydroxide to bring the pH of the solution to 2 and dilute the solution to 25ml with water.

Shake well and centrifuge for 5 minutes. Separate the clear supernatant layer and allow it to stand in a room temperature until the pH stabilizes. If the pH is not between 2.3 and 3.5, repeat the test using a different volume of 0.1N sodium hydroxide. Use the clear supernatant layer.

Sample injection procedure

50µL of filtered sample solution and standard solution were separately injected into the HPLC system. The chromatogram was recorded and the responses were measured for the major peaks. The content of Sucralfate per tablet was calculated using the following expression.

Content of Sucralfate per tablet

$$= \frac{AT}{AS} \times \frac{Wstd}{5} \times \frac{25}{Wsample} \times \frac{974.75}{1287.53} \times \frac{100 - \%\text{ of water content of std}}{100} \times \frac{p}{100} \times \text{Av. Wt of tablet}$$

Where,

AT = Area of sample solution, AS = Area of standard solution.

W_{std} = Weight of standard, W_{sample} = Weight of sample.

P = Percentage purity.

***In Vitro* Dissolution Study**[10]

Preparation of standard solution

Weigh accurately about 6.4 mg of potassium sucrose octasulfate reference standard in dried stoppered flask and add 10 ml of mobile phase. Sonicate for 5 minutes and dissolve well.

Preparation of sample solution

The release of Sucralfate chewable tablet was studied in 900ml of 0.1N HCl/0.067 M KCl as dissolution medium using USP dissolution apparatus type II (paddle) at a speed of 75 rpm maintained at 37°C±0.5°C. One tablet was placed in each jar. The apparatus was run and 20 ml of sample was withdrawn at 5, 10, 15, 20 and 25 minutes. From this 5ml of the filterate was diluted to 25 ml with mobile phase. The resultant solution was filtered through membrane filter and analyzed for percentage drug release by HPLC method.

Sample injection procedure

50 µL of filtered portion of the standard solution and sample solution were separately injected into the HPLC system. The chromatogram was recorded and the responses were

measured for the major peaks. The amount of drug release was calculated in percentage with respect to label claim by using the following expression.

$$\text{Drug release} = \frac{AT}{AS} \times \frac{WS}{10} \times \frac{900}{1} \times \frac{25}{5} \times \frac{P}{100}$$

Where,

AT = Area of sample solution, AS = Area of standard solution

WS = Weight of standard solution, P = Percent purity of Sucralfate

$$\%\ \text{Drug release} = \frac{\text{mg of drug released}}{\text{label claim}} \times 100$$

FT-IR Spectral Analysis[12]

Fourier transform infrared (FT-IR) study was carried out to determine any interaction between drug and excipients. FT-IR analysis of pure drug and drug + excipients was taken for the study. Samples were compressed with potassium bromide and transformed into disk. Disk was applied to the center of the sample holding device and scanned between 2000 - 400 cm^{-1} in a SHIMADZU FT-IR (IR affinity-1) spectrophotometer.

Stability Study[13]

The best formulation was packed in high density polyethylene container and kept at $40^0C \pm 2^0C/75\% \pm 5\%RH$ for 3 months. Samples were visually examined for any physical changes and evaluated for drug content, disintegration time, acid neutralizing capacity and *in vitro* dissolution study at an intervals of 1, 2 and 3rd month.

RESULTS AND DISCUSSION

Precompression Parameters

The prepared Sucralfate granules were evaluated for the pre-compression parameters, such as bulk density, tapped density, compressibility index, Hausner's ratio and angle of repose. The results revealed that the formulations SCT-5, SCT-6 and SCT-7 showed excellent flow property in terms of micromeritic parameters. The results are presented in Table 2.

Table 2: Precompression Parameters

S. No	Formulation code	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's index (%)	Hausner's ratio	Angle of repose (Θ)
1	SCT-1	0.50±0.001	0.625±0.002	20.0±0.20	1.25±0.25	$32^0.54'$±0.15
2	SCT-2	0.525±0.002	0.625±0.003	16.0±0.20	1.19±0.20	$31^0.72'$±0.09
3	SCT-3	0.512±0.003	0.518±0.002	23.74±0.16	1.31±0.14	$31^0.26'$±0.34
4	SCT-4	0.391±0.001	0.511±0.001	23.48±0.13	1.30±0.14	$34^0.40'$±0.17
5	SCT-5	0.506±0.002	0.586±0.001	13.65±0.14	1.15±0.30	$30^0.64'$±0.14
6	SCT-6	0.502±0.004	0.573±0.003	12.40±0.14	1.14±0.20	$30^0.16'$±0.30
7	SCT-7	0.498±0.004	0.568±0.003	12.32±0.20	1.14±0.30	$30^0.84'$±0.10

***All values are expressed as mean±SD, n=3**

EVALUATION OF SUCRALFATE CHEWABLE TABLETS

Postcompression Parameters

The compressed tablets were evaluated for various parameters such as thickness, hardness, friability, weight variation, disintegration time and drug content. The thickness of the tablets was found in the range of 4.17±0.09 to 4.84±0.11 mm. All the formulations showed uniform thickness. The hardness of Sucralfate chewable tablets were found in the range of 2.0±0.10 to 5.2±0.08 kg/cm^2. Formulation SCT-1, SCT-2 and SCT-3 possessed less mechanical strength with hardness in the range of 2.0±0.10 to 3.5±0.03 kg/cm^2. Formulation SCT-4, SCT-5, SCT-6 and SCT-7 possessed good mechanical strength with hardness in the range of 3.8±0.06 to 5.2±0.08 kg/cm^2. In friability test the percentage weight loss of Sucralfate chewable tablets was found to be within 1% in the formulations SCT-4, SCT-5, SCT-6, SCT-7 and hence passed the friability test. Other formulations (SCT-1, SCT-2 and SCT-3) failed in friability test. All the formulations showed acceptable limits and complied with I.P specifications for weight variation. The disintegration time of Sucralfate chewable tablets were found between 48 to 96 seconds. All the formulations disintegrated within the time as specified in the USP. Formulation SCT-7 showed rapid disintegration compared with other formulations. The assay values were found in the range of 99.12±0.04 to 100.18±0.04 for all formulations, which was within the acceptable USP limits. The results are presented in Table 3.

Table 3: Evaluation of Sucralfate Chewable Tablets

Formulation code	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight variation (mg)	Disintegration time (sec)	Assay (%)
SCT-1	4.84±0.11	2.00±0.10	4.43±0.02	1800±0.35	96±0.2	99.12±0.04
SCT-2	4.64±0.10	3.50±0.03	2.32±0.01	1775±0.35	80±0.12	99.92±0.08
SCT-3	4.71±0.11	3.0±0.10	2.10±0.04	1802±0.03	77±0.17	100.12±0.07
SCT-4	4.17±0.09	4.0±0.06	0.87±0.01	1600.1±0.10	60±0.25	99.16±0.06
SCT-5	4.34±0.09	3.80±0.06	0.84±0.01	1600.3±0.05	62±0.26	99.12±0.06
SCT-6	4.41±0.09	5.0±0.09	0.33±0.01	1675.8±0.04	57±0.15	100.18±0.04
SCT-7	4.56±0.09	5.2±0.08	0.32±0.02	1690±0.07	48±0.03	100.16±0.06

***All the values are expressed as mean±SD, n=3**

The bitter taste of the drug was changed in all formulations by using sugar free sweetening agents. All the formulations possessed sweet taste. The prepared tablets were found to be pale orange in colour. Acid neutralizing capacity of Sucralfate chewable tablets were found in the range of 16.3 - 17.44 mEq. USP specification for acid neutralizing capacity is not less than 12.0 mEq. Hence all formulations passed in acid neutralizing capacity. Among all formulations SCT-7 showed good acid neutralizing capacity. The acid neutralizing capacity of Sucralfate chewable tablets were shown in table no.4 and fig: 1.

Table 4: Acid Neutralizing Capacity of Sucralfate Chewable Tablets

S. No	Formulation Code	Acid Neutralizing Capacity (mEq)
1	SCT-1	16.4±0.06
2	SCT-2	16.6±0.08
3	SCT-3	16.3±0.09
4	SCT-4	16.7±0.05
5	SCT-5	16.5±0.10
6	SCT-6	17.1±0.15
7	SCT-7	17.44±0.04

***All the values are expressed as mean±SD, n=3**

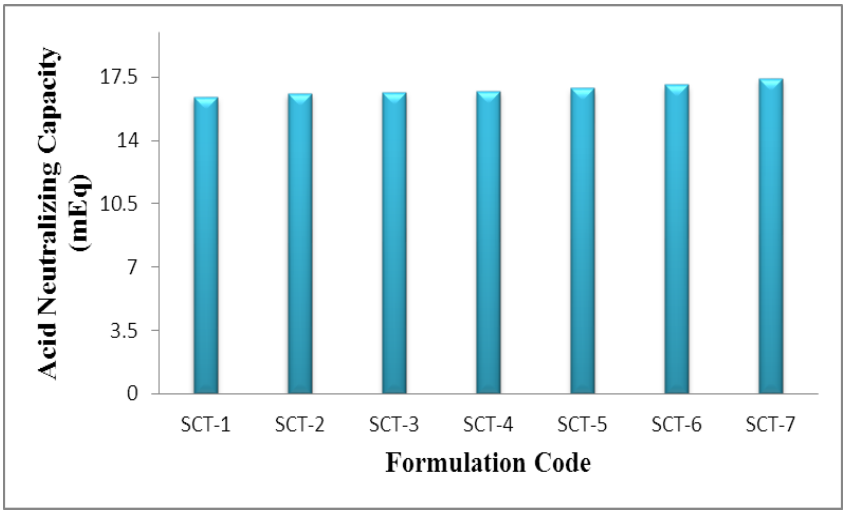

Fig. 1: Acid Neutralizing Capacity of Sucralfate Chewable Tablets.

In the dissolution study, formulation SCT-7 showed 92.3% drug release at the end of 25 minutes and the percentage drug release was found to be better than all other formulations. The results of *in vitro* drug release studies are presented in table 5 and the drug release profiles were shown in fig. 2.

Table 5: Dissolution Data of Sucralfate Chewable Tablets

Time	Percentage Drug Release (%)						
(min)	SCT-1	SCT-2	SCT-3	SCT-4	SCT-5	SCT-6	SCT-7
5	8.39±0.11	13.34±0.34	12.75±0.16	18.67±0.19	17.64±0.15	18.45±0.19	18.74±0.09
10	17.40±0.33	22.33±0.50	24.59±0.20	29.40±0.13	31.26±0.34	35.20±0.22	37.73±0.22
15	38.67±0.31	43.67±0.17	46.51±0.23	52.7±0.088	51.14±0.22	56.52±0.17	62.55±0.05
20	54.38±0.19	62.76±0.17	64.46±0.17	74.64±0.094	76.63±0.23	79.48±0.10	81.66±0.05
25	73.23±0.28	78.49±0.11	77.48±0.11	83.55±0.14	85.60±0.13	88.36±0.08	92.3±0.09

***All the values are expressed as mean±SD, n=3**

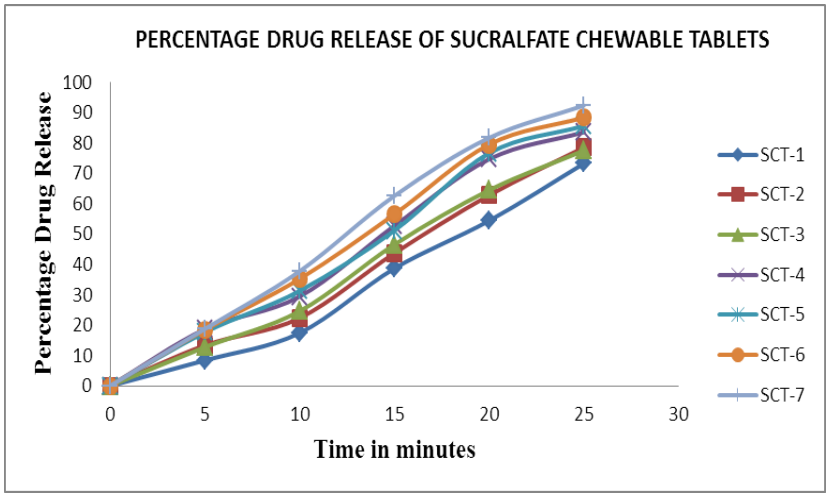

Fig 2: *In Vitro* Drug Release Profiles of Sucralfate Chewable Tablets.

Formulation SCT-7 showed rapid disintegration among all formulations (48±0.03 seconds). This formulation also possessed good hardness than all formulations (5.2±0.08 kg/cm^2) and also showed better acid neutralizing capacity (17.44 mEq) compared to all other formulations. The formulation SCT-7 showed 92.3% drug release at the end of 25 minutes. The percentage drug release was also found to be better than all other formulations. Hence based on rapid disintegration time, good mechanical strength, better acid neutralizing capacity and rapid drug release amongst all formulations, the formulation SCT-7 was selected as best formulation.

The FT-IR spectrum of formulation (SCT-7) showed all the characteristic peaks of Sucralfate, thus confirming that no interaction of drug occurred with the components of the formulation. Stability study results revealed that there were no significant changes found in appearance, disintegration time, drug content, acid neutralizing capacity and *in vitro* drug release during the period of 3 months even after stored at 40^{0}C±2^{0}C/75%±5%RH. The results of stability study revealed that the drug was stable even after stored at 40^{0}C±2^{0}C/75%±5%RH for 3 months. The stability study results of best formulation are given in Table 6.

Table 6: Stability Study Results of Best Formulation (SCT-7)

Parameters	**Storage Condition: 40^{0}C±2^{0}C/75%±5%RH**			
	Initial period	**1st month**	**2nd month**	**3rd month**
Colour	Pale orange colour	Pale orange colour	Pale orange colour	Pale orange colour
Disintegration time (sec)	48±0.03	48±0.04	49±0.01	49±0.03
Drug content (%)	100.16±0.06	100.02±0.02	99.98 ±0.01	99.96±0.02
Acid neutralizing capacity(mEq)	17.44±0.01	17.42±0.03	17.40±0.01	17.38±0.03
***In Vitro* drug release after 25 minutes (%)**	92.31±0.03	92.28±0.2	92.25±0.14	92.23±0.08

***All the values are expressed as mean±SD, n=3**

CONCLUSION

From the above study, the overall results revealed that the formulation SCT-7 containing combination of two superdisintegrants (croscarmellose sodium and sodium starch glycolate) was found to be the better one which satisfied all the criteria for chewable tablets. Thus it was concluded that sugar free Sucralfate chewable tablets could be successfully formulated by wet granulation method using superdisintegrants such as croscarmellose sodium and sodium

starch glycolate, thereby improving the patient compliance, convenience in administration and therapeutic effectiveness of Sucralfate and making it suitable for diabetic and non diabetic patients.

ACKNOWLEDGEMENT

The authors thank Research and Development Department of Fourrts (India) Laboratories Pvt. Ltd, Kelambakkam and Thiru. S. Sriram Ashok, Correspondent of Sankaralingam Bhuvaneswari College of Pharmacy for providing necessary facilities to carry out this work.

REFERENCES

1. Mullarney MP. The powder flow and compact mechanical properties of sucrose and three high intensity sweeteners used in chewable tablets. Int. J. Pharm, 2003; 4(3): 227-236.
2. Lachman L, Liberman HA, Schwartz JB. Pharmaceutical dosage forms. 3rd ed., New York; Marcel Dekker Inc, 1989; 112-117.
3. Lachman L, Liberman HA, Kanig LJ. Theory and Practice of Industrial Pharmacy. 3rd ed, New Delhi; Vargese Publication House, 1990; 293-336.
4. http://drugsdetails.com/sucralfate-uses-dosage-mechanism-of-action-side-effects.
5. Martin A, Swarbrick J, Cammarata A. Physical Pharmacy, 2nd ed, USA; Wolters Kluwer, 1983; 532-533, 513-551.
6. Carr RL. Evaluation of flow properties of granules. Chem. Eng, 1965; 72: 163- 168.
7. Gregory E Amidon, Pamela J Secreast, Deanna Mudie. Particle, Powder and Compact Characterization. In: Yihong Qui, Yisheng Chen, Geoff GZ Zhang. Developing solid oral dosage forms. 1st ed; USA; Elsevier, 2009; 168-169.
8. Shishu, Ashima bathi and Tejbor Singh. Preparation of tablets rapidly disintegrating in saliva containing bitter masked granules by compression method. Indian J. Pharm. Sci, 2007; 69: 80-84.
9. Nagendra kumar D, Raju SA, Shirs and Params SB. Design of fast dissolving Granisetron HCl tablets using novel coprocessed superdisintegrants. Int. J. Pharm. Sci. Rev. Res, 2010; 12: 58-62.
10. The United State of Pharmacopoeia 2-NF 1 Supp.3, United States Pharmacopoeial Convention Inc; Rockvile, 2006; 2: 54-55.
11. The United State Pharmacopoeia XXV, United States Pharmacopoeial Convention Inc; Rockvile, 2002; 1: 956-958.

12. Vijayanand P, Patil JS and Venkta reddy M. Formulation and evaluation of orodispersible tablets of Nebivolol HCl, Int. J. Pharm. Sci, 2011; 38: 323-332.
13. Stability testing of active substances and pharmaceutical products. World Health Organization, 2006; CH-1211; 27: 12-30.