Journal of
Community & Public Health Nursing
Research Article Open Access

Formulation and Evaluation of Antihypertensive Chewing Gum of Irbesartan

Roshan Kumar Dubey*

Lifecare Neuro Products Limited, Baddi, Himanchal Pradesh, India

Abstract

Pharmacologically active agents can be made in various dosage forms such as tablets, capsules, syrups, injections, inhalers, ointments and creams. In the oral cavity a huge number of medically active agent integrated, and in the last some years, there has been a scientific and technological advance in the advancement of oral delivery systems. Chewing gum is a flexible delivery system that favours a wide range of pharmacologically active ingredients and allows faster therapeutic action than every oral dosage form.

Keywords: Chewing gum; Tablets; Capsules; Syrups; Injections; Inhalers; Ointments

Introduction

Medicaid chewing gum (MCG) is defined by the European Pharmacopoeia and in 1991, and the guidelines for drug doses were issued for human use 'solid single dose preparations with a base containing mainly gum. It is meant to chew. But not swallowed, releasing slowly and steadily". MCG is a solid single-dose form of mastic gum core that contains clinically active ingredients, polymers, waxes, flavours or colours in the core, coating or both. MCG is currently available for smoking cessation, pain relief, motion sickness and breathing freshness [1,2].

Candidates selected as MCG should have physicochemical properties such as high salinity solubility, pH-dependent solubility, tastelessness, without affecting salivary flow rate and patient-related factors (Oromocosa and salivary tubes, non-toxic to non-cancerous Is and should not cause tooth) decay [3] The rate of active release from chewing gum is determined by the physicochemical properties of the drug, composition and preparation process, and by the patient's chewing performance. She goes. Patient chewing performance. This means that different chewing times, chewing frequency, chewing intensity, and patients with xerostomia or oromucosal diseases may experience different chewing performance [4,5]. The amount of chewing drug depends on the mechanical chewing activity, the amount of chewing power. And chewing intensity Particle size should be kept below 100 μm to prevent unpleasant pesky feeling during chewing, while chewing. The process, drug residue in the gums, is released from the saliva product and is absorbed into the stomach by the oral mucosa or for gastro-intestinal absorption [6]. The aim of the present work was to develop and develop sugar-free chewing gum delivery of irbursan (IRB) and atorvastatin for the treatment of hypertension and to evaluate important formulation parameters of MCG.

Materials and Methods

Materials

Irbesartan, fine dry powder of glycerrhiza, paraffin wax, glycerin, olive oil, and castor oil and Gum base of food grade were supplied by Yellow Chem Pharma Products, Mumbai. Atorvastatin was purchased from Cipla Pharmaceutical Indore. Green colour of food grade was purchased from market. Most of the chemicals used in research were of analytical grade.

Method

Identification test by UV spectroscopy: Accurately amount like 10 mg of Irbesartan solution was prepared in 100 ml of volumetric flask, and diluted up to marks with methanol and to give a stock solution having 100 μg/ml strength. Similar procedure was performed for the atorvastatin. Pipette out 0.5, 1.0, 1.5, 2.0, 2.5 and 3.0 ml of the stock solution of Irbesartan and Atorvastatin into a series of 10 ml volumetric flask and volume was maintained by methanol up to the mark. Further absorbance was measured at 226 and 246 nm, and graph was plotted between absorbance *vs* concentration of Irbesartan and Atorvastatin. Linearity range of Irbesartan and Atorvastatin was found with correlation coefficient.

Formulation: MCG is prepared by the traditional method. A total of nine formulations were prepared in this study, including MCG 1,2,3 formulations with glycerin, 6 formulations with castor oil and MCG 7,8,9 formulations with olive oil (Table 1). First, the synthetic gum base and paraffin wax were melted in a steam bath at 35-45 ONC in a porcelain dish. Second, add the softened amounts of glycerin, castor oil and olive oil to this dissolved mass and then mix well. The mixture was allowed to cool to a temperature of 15–20 K, and then IRB, atorvastatin, talc (anti-adjuvant) and glycuriza (as a sweetener) were used to determine delivery. Used. Added to constant confusion.

Finally, the orange flavor and color are added. The gum mass was allowed to cool for 48 hours on a steel plate at a controlled temperature so that the gum mass was properly set, then the gum mass was spread evenly and finally the required mass was cut into slices and the pieces were carefully given. Cold controls temperature and humidity. The net weight of each chewing gum is 2 g (Table 1).

Characterization of Medicated Chewing Gum

Physical evaluation

The colour, appearance, stickiness, hardness and weight variation all type of formulation were physically evaluated [7, 8]. The colour and appearance was measured by visual observation.

Stickiness: The MCG was placed on a flat surface, and the Teflon hammer (250 g) was struck at a frequency of approximately 30/min for ten minutes. The stickiness of the mass to hammer the surface was not observed and was reported 10 minutes later [7,8].

***Corresponding author:** Roshan Kumar Dubey, Lifecare Neuro Products Limited, Baddi, Himanchal Pradesh, India, Tel: +91 9532358980, E-mail: Pharamaroshan95@gmail

Received February 06, 2021; **Accepted** March 08, 2021; **Published** March 15, 2021

Citation: Dubey RK (2021) Formulation and Evaluation of Antihypertensive Chewing Gum of Irbesartan. J Comm Pub Health Nursing 6: 274.

S. N.	Ingredients	F-1	F-2	F-3	F-4	F-5	F-6	F-7	F-8	F-9
1	Irbesartan	25	25	25	25	25	25	25	25	25
2	Atorvastatin	10	10	10	10	10	10	10	10	10
3	Gum base	500	500	500	500	500	500	500	500	500
4	Glycerin	100	200	300	-	-	-	-	---	---
5	Castor oil	-	-	-	100	200	300	-	---	---
6	Olive oil	-	-	-	-	-	-	100	200	300
7	Paraffin wax	100	100	100	100	100	100	100	100	100
8	Talc	100	100	100	100	100	100	100	100	100
9	Glycerrhiza	1045	945	845	1045	945	845	1045	945	845
10	Flavouring agent	100	100	100	100	100	100	100	100	100
11	Colour agent	20	20	20	20	20	20	20	20	20

Table 1: Different formulation and its ingredients ratio (weight in mg).

Hardness/Plasticity: Due to lack of the method of hardness and plasticity determination Monsanto Type Hardness Tester was used for all the medicated chewing gum formulation [7, 8].

Weight variation: According to the some reference article method weight variation of all the formulation was done. Randomly 10 chewing gum was taken. Unit weight of each further average weight calculated. Then standard deviation was calculated [7-9].

Drug content: Randomly selected three chewing gum and each gum was dissolved in 100 ml of PBS having pH 6.8. The amount of Irbesartan and Atorvastatin were analysed by measuring the absorbance at 226 and 246 nm by UV spectroscopy.

In-vitro drug release

Apparatus I. **Chewing gum apparatus**: Compendial-Ph. Eur.

The chewing device consists of a chewing chamber, two horizontal pistons and a vertical piston (tongue). The vertical piston alternates with the two horizontal pistons to ensure that the gum between the chips is in the correct position. If necessary, the horizontal piston at the chewing end rotates in opposite directions around its axis for maximum chewing. Chewing process for in vitro drug release based on [10-12].

1) Change from 5-30°C to the twisted angle of the upper mastication jaw.

2) Change the b/w distance in the upper and lower mastic from 1-2 mm to the jaw.

3) Changes in the frequency of low masticating jaws range from 20 strokes per minute to 120 strokes per minute.

4) Temperature varies from 30-40°C. The chewing process involves lower and lower strokes of the lower masticating surface, with less movement of the upper masticating surface for chewing gum, reducing the chewing frequency received from 60 to 2 strokes per minute. The piston is placed between the chewing surfaces. Artificial saliva particles were removed at predetermined intervals and analyzed for residual material using a UV spectrophotometer. After each sample was taken, the release medium was replaced with fresh artificial saliva [13-15].

Stability study

According to WHO guideline for stability studies, at temperature of 30±02 °C and relative humidity of 65% ± 5%, 10 gram of synthetic gum base was stored in bottle for the six months. Natural ageing and physical nature was examined after the six months [7].

Fourier transform infrared spectroscopy (FTIR)

Drugs and synthetic glue base interactions were observed using FTIR (Shimadzu Japan). Sample preparation was performed on a KBr disk (2 mg sample in 200 mg KBr). Scanning range, resolution and hydraulic pressure were kept at 400–4000 cm -1, 2 cm -1 and 150 kg/cm 2, respectively. IR Spectra has been recorded for pure drugs (IRB and atorvastatin), pure synthetic gum base, combination of drugs (IRB and atorvastatin), and drugs and synthetic gum base (IRB, atorvastatin and synthetic gum base) [9].

Contact time

MCG contact time is responsible for local or systemic effects in the oral cavity. In the clinical trial, normal chewing time was assumed to be 30 min. Four healthy volunteers were selected for this study. Everyone was allowed to chew the piece of MCG as long as possible so that its maximum risk remained in the oral cavity, and this was observed when the volunteers took the MCG out of the drum.

In-vivo study on healthy volunteers

Buccal absorption test: Test was done by introducing each concentrate solution (25 mL) into a different concentration; For the IRB (0.5 mg/ml) and atorvastatin (0.4 mg/ml), the mean oral dose of a human volunteer was 1.2, 4.5, 5, 6, 6.5, 7, 7.5, 7.8, with 8 different pH values. Swallowed it in the buccal cavity for 15 minutes and then kicked. The excreted saliva was analysed with IRB at 230 nm and atorvastatin at 246 nm against the blank factor by the UV spectrophotometric method [16].

Release of drug in saliva: In this method, all the aggregates of Che Gumming with saliva are selected to release sal saline into the saliva. Four human volunteers (two men and two women) were instructed to rinse their mouths with distilled water and allowed to chew gum for 15 minutes. Saliva sample was taken 5 min later, followed by 2, 4, 6, 8, 10,12,14 and 15 min. Saliva samples were dissolved in phosphate buffer (pH 6.8) and analyzed by UV spectrophotometric method against UR reagent for IRB and atorvastatin at 247 nm to 230 nm [17].

Dissolution test of residual medicated chewing gum

In the present experiment, a group of volunteers examined the gums to verify the release process from the delivery system. A sample of gum was chewed on each person for different time periods (1,5,10,15 minutes). The residual gums are cut into small pieces, frozen to a fine powder, and then laid on the ground. Residual drug content was determined using a dissolution test procedure (U.S.P. soluble test apparatus, at 100 rpm and 37°C) by a UV spectrophotometer. The amount of residue of the glue that is released during mastication

is calculated by subtracting the total content of the residual active substance in the glue [18].

Urinary excretion profile of medicated chewing gum

Four healthy volunteers were selected and given strict instructions not to take any medications in the last 48 hours and not to empty their bladder in a volumetric flask. Sample collection began at 0, 15 min and 1, 2, 3, 4, 6, 7, 8, 10, 11, 12 and 24 hours after chewing gum administration. Volunteers were asked to drink water for 30 minutes. The samples were analyzed by UV absorption spectrophotometer at 230 nm for IRB and at 247 nm for atorvastatin against the vacuum reagent [19].

Results and Discussion

Identification test

In the medium phosphate buffer pH 6.8, a λ_{max} for IRB and Atorvastatin was found to be 230 nm and 246 nm respectively. The calibration curve were prepared from stock solution (0.5, 1.0, 1.5, 2.0, 2.5, 3.0 µg/mL). The linear line is observed with regressions coefficient were found to be 0.992 and 0.994. Total nine batches were prepared having different concentration of glycerin, castor oil, olive oil and glycerrhiza.

Physical evaluation

Physically evaluated data of Colour, Appearance, Stickiness ad Hardness was prescribed in Table 2.

Stickiness

Negligible Stickiness of all formulations was found. It shows the better patients compliance, because drugs release from MCG very smoothly (Table 3).

Weight variation

The obtained average weight of 10 MCG was found to be 1.97gm. While net weight of each chewing gum was 2gm and it was within normal range.

Drug content

It was found to be between 91% and 96% and the average value was 93.01, which is within the normal range. Homogeneity in content content was found in all formulations such as IRB (25mg) and atorvastatin (10 mg) (Table 2).

In-vitro drug release

More than 15% of all aggregate releases were found after 15 min. These findings indicate the oral presence of MCG in the oral cavity and the graph shows the comparative release rate of all aggregates at 30 min. MCG 6 formulation has been found to show better release than other aggregates. Therefore, MCG6 formulation was selected as the best batch and came forward for its stability study. As a twisting angle motion for the twisted jaw, the optimized alignment of the twisted angle was found at 20 min, 99 min after 29 min of release, indicating that increasing the twisting angle would significantly increase the release shaft release rate. Gone. The chewing frequency of the lower masticating jaw is an important part of the mastication process because chewing the release profile reflects a significant increase or increase in the speed of the lower masticating movement. Reducing the distance between the upper and lower mastic surface from 2 mm to 1 mm increases the release rate in all aggregates because the force acting on the glue is larger than the 1 mm setting. Excessive muscle twisting between the jaws of the chewing device leads to an increase in the release rate and a decrease in the release time. The release does not have a significant effect on the overall profileas we increase the temperature from 30-40 from C. Formulation MCG 6 is the best formulation of castor oil as P value shows (Tables 3, 4 and Figure 1).

Go to the selected batch F-5 and characterization, according to the results of the study of physical properties, content drug content and in vitro drug release (Figures 2).

Stability study

The stability studies of MCG confirm that there is no change in the physical appearance, the point of softening the color and glue of the stored samples is the stability studies of MCG (Table 3).

Fourier Transform Infrared Spectroscopy (FTIR) Results

Taken in combination with the FTIR spectra and synthetic glue base of IRB and atorvastatin. FT-IR spectra of pure atorvastatin calcium 2955.15 cm-1 (CN-stretching), 3059.15 cm-1 (CH-stretching), 1313.56 cm-1 (C-HO-stretching alcohol group), 1564.97 cm. your Shown. 1 (C=O -Stretching Amidic group), 3403.27 cm -1 (NH-Stretching),

Formulations	Colour	Appearance	Stickiness	Pressure required to press gum (kg/cm2)	% drug content
F-1	Dark green	Hard	Nil	2.1	91.32
F-2	Light Green	Hard		2.6	90.58
F-3	Green	Soft		2	93.61
F-4	Green	Hard		2.3	95.98
F-5	Dark green	Soft	Negligible	1.4	96.49
F-6	Light Green	Soft		1.6	91.05
F-7	Green	Hard	Nil	1.5	93.67
F-8	Light green	Soft		2.2	91.95
F-9	Dark green	Hard	Negligible	2.1	92.49

Table 2: Physical characteristics of all prepared formulations.

Color	before aging	Off white-light yellow
	after aging	
Softening range	before aging	87-92°C
	after aging	
Texture	before aging	Gummy
	after aging	

Table 3: Physiochemical properties of synthetic gum base after stability Studies.

pH of buffer solution (F-5)	5	5.5	6	6.5	7	7.5	8
% drug absorbed	67.43 ± 0.14	81.59± 0.11	73.89± 0.51	71.92 ± 0.46	66.51 ± 0.26	59.15 ± 0.26	53.48 ± 0.21

Table 4: Buccal absorption test at different pH of formulation F-5 containing castor oil.

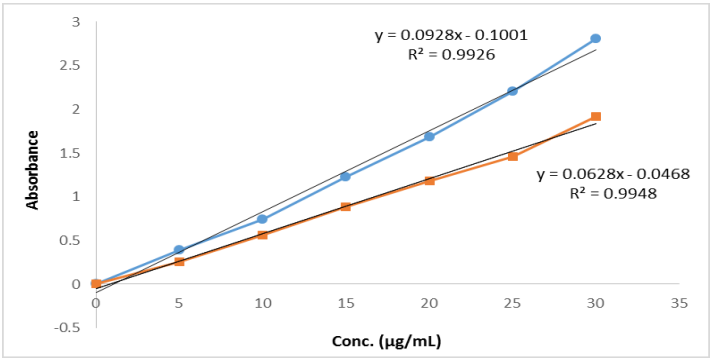

Figure 1: Standard calibration curve of Irbesartan and Atorvastatin.

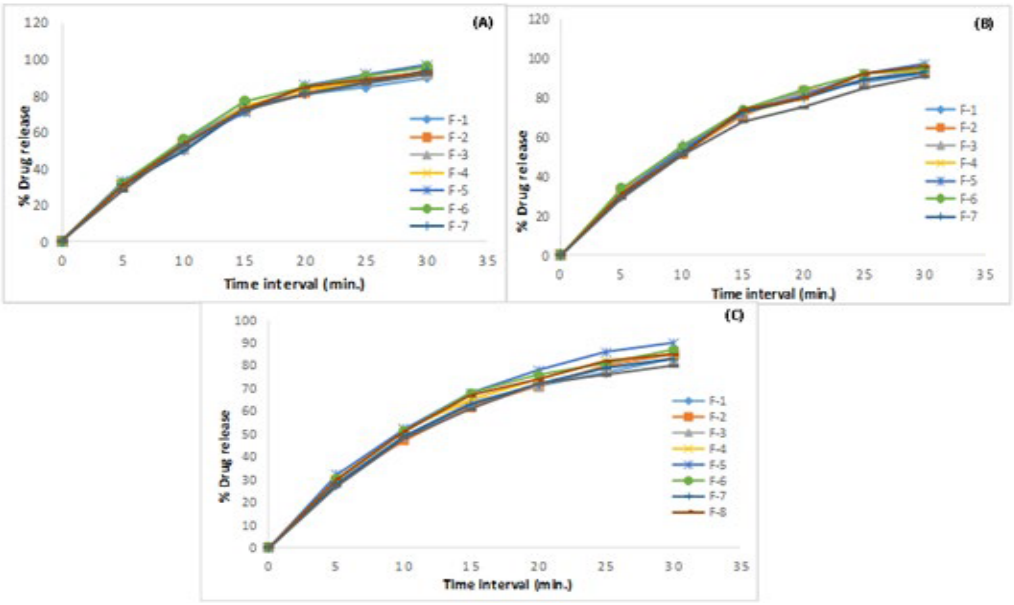

Figure 2: A) In vitro drug release with chewing frequency setting of 60 strokes/minute B) In vitro drug release with distance setting between the jaws 1.5 mm C) In vitro drug release with setting of twisting angle at 5°c.

1656.97 cm -1 (C=C -Bending), 751.62 cm-1, 696.95 cm .M -1 (cf-stretching), 1104.39 cm. -1 (OH-bending). This may be a possibility of intermolecular hydrogen bonding between adjacent atorvastatin calcium molecules. The spectrum of pure atorvastatin calcium was compared with the spectrum obtained in combination with a synthetic glue base [20]. The IRB of the IRB is characterized by the absorption of the NH group at 2958 cm-1. A similar absorption spectrum of IRB was obtained. When At Shadhan was combined with IRB and synthetic gum base, no significant change in the IR peaks of atrovastatin calcium was observed. These observations indicate the compatibility of atorvastatin calcium and IRB with each other, as well as the compatibility of atorvastatin calcium and IRB with synthetic gum bases (Figure 3) [21-23].

Contact time

In oral cavity best contact time of MCG 5 with castor oil softener was 28 minutes. Castor oil provides smooth mastication. The average contact time of the MCG was found to be 26 min.

In vivo study on healthy volunteers

These results prove that there is a good governance system for governance in the form of chewing gum. Dosage form release is an important step and its bioavailability is very limited, with only a small percentage of the amount of chewing gum being released, but the bulk of the dose occurs during delivery. As a medical necessity, MCG has been shown to give rapid and complete release conditions after relatively low chewing. The total amount of MCG in the dosage form is distributed after the time (1 min) and there is no significant increase in the recovery rate from the fog queues, which is evidence of an increase in mastification time. From a comparative point of view, castor oil is in the gum formula because plasticizers provide good dosage against glycerol and olive oil combinations. From a revised release study on healthy volunteers, glycerol F-3, castor oil F-6 and olive oil F-8 were found to have good stability in drug formulation and salinity rapid release, but castor oil was obtained by others. F-5K is believed to show optimal results against 15 minutes of IRB chewing and crushing and

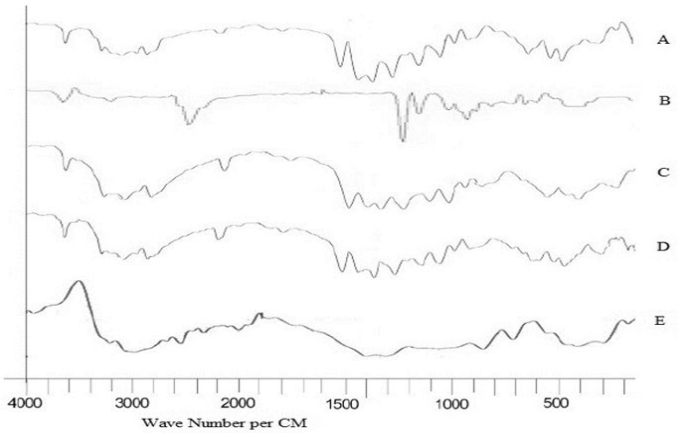

Figure 1: Standard calibration curve of Irbesartan and Atorvastatin.

finely mixing aerovastatin aggregates, which are believed to have a pH for which more than 80% of the drug is absorbed into the buccal cavity, which is considered average. Time to chew gum. Therefore, the therapeutic product absorption is immediately available because there are no significant differences between these quantities obtained after 10-15 minutes of chewing. Castor oil preparation as a plaster sizer releases almost all activators in a very short amount of time (11 minutes), as different formulas can be explained by looking at the active formulas and the different concentrations of plasticizers. Therefore, the release rate depends on the solubility and nature of the water and the ration of the plasticizer.

Data on urination showed that excretion from the first pass effect of the first stroke in a short period of time (2 hours). The buccal absorption test revealed that more than 80% of the drug content was absorbed within 15 minutes when the bouquet mucus was obtained at pH 5.5.

Conclusion

Therefore, Choo gum of IRB and atorvastatin is considered to be a good, fast and novel formulation for buccal drug delivery systems to avoid first-pass effects, overdose, easy administration and reduce the risk of rapid action.

References

1. Athanikar NK, Gubler SA (2001) Process for manufacturing a pharmaceutical chewing gum. 2001; US Patent. 6322828.
2. Committee for Medicinal Products (1991) CPMP list of allowed terms for the pharmaceutical dosage form, route of administration, container, closure and administration devices. Brussels. Belgium III, 35:91-93.
3. Jacobsen J, Christrup LL, Jensen NH (2004) Medicated Chewing Gum: Pros and Cons. Am J Drug Deliv 2(2):75-88.
4. Logemann JA (2004) Effects of xerostomia on perception and performance of swallow function. Head Neck 23:317-321.
5. Liedberg B, Owall B (1991) Masticatory ability in experimentally induced xerostomia. Dysphagia 6(4):212-213.
6. Amposta R (2010) Medicated Chewing Gum. Pharma Technology Euro 22(1):1-22.
7. Sarfraz RM (2016) Comparative Study of Various Polymeric Superdisintegrants on the Design and Evaluation of Novel Antihypertensive Orodispersible Tablets. Adv poly technol 35:378-385.
8. **8** Asif M (2015) Development and In Vitro Evaluation of Acyclovir Rapid Dissolving Tablets: a Solubility and Bioavailability Enhancement Study. Lat Am J Pharm 34(9):1701-1709.
9. Sarfraz RM (2015) Formulation and Evaluation of Mouth Disintegrating Tablets of Atenolol and Atorvastatin. Indian J pharm Sci 77(1):83-90.
10. European Directorate for the Quality of Medicines (2000) Council of Europeeuropean pharmacopoeia. (3rd ed.), Strasbourg, France.
11. European Directorate for the Quality of Medicines (2005) Council of europeeuropean pharmacopoeia. Suppl 5.2 general monograph 2.9.25 dissolution test for medicated chewing gums (5thed.) Strasbourg,France, 3116-3117.
12. European Directorate for the Quality of Medicines (2008) Council of europeeuropean pharmacopoeia. General monograph 2.9.25 dissolution test for medicated chewing gums (6th ed.) Strasbourg, France, 304-306.
13. Subraman R (2002) Medicated chewing gum delivery system for nicotine.US Patent 6344222B1.
14. Shojaei AH, Bret B, Xiaoling L (1998) Transbuccal Delivery of Acyclovir: I. in Vitro Determination of Routes of Buccal Transport. Pharm Res 15(8):1182-1188.
15. Hughes L (2003) Buccal dissolution of active substances. US Patent 20030087457A1.
16. Beckett AH, Triggs EJ (1967) Buccal absorption of basic drugs and its application as an in-vivo model of passive absorption drug transfer though lipid membranes. J Pharm Pharmacol:19:31-41.
17. Dong C, Jr Puckett AD, Dawes C (1995) The effect of chewing frequency and duration of gum chewing gum on salivary flow rate and sucrose concentration. Archiev Oral Biol 40(7)**:**585-588.
18. Maggi L (2005) Preparation and evaluation of release characteristics of 3TabGum, a novel chewing device. EurJ PharmSci 24(5):487-493.
19. Upendra N (2010) Formulation of medicated chewing gum of Ondansetron hydrochloride and its pharmacokinetic evaluations. Int J Pharm Sci Tech 1(2):33-40.
20. Sarfraz RM (2014) Formulation and in-vitro evaluation of novel atorvastatinamlodipine orodispersible tablets. Int J Bio Pharm Sci 3(6):941-951.
21. Jagdale S, Ghorpade S, Bhavsar D, Kuchekar B, Chabukswar A (2010) Effect of wax on the release pattern of drugs from the sustained release fatty matrix tablet. J Chem Pharm Res 2(2):330-338.
22. Tayade TP, Kale DR (2004) Encapsulation of water insoluble drug by a cross linking technique: effect of process and formulation variables on encapsulation efficiency, particle size and in vitro dissolution rate. AAPS Pharm Sci 6(1):112-119.
23. Naik H, Gupta S (2010) Medicated chewing gums-updated review. Int J Pharm Res Dev 2(8):66-76.