EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 1
293-297
Year: 2021

DEVELOPMENT AND EVALUATION OF MEDICATED CHEWING GUM CONTAINING ONDANSETRON HYDROCHLORIDE

Suraj Yadav[1*], Sandeep Atram[2], S. D. Pande[2] and Nishan N. Bobade[2]

[1]Dr. Rajendra Gode College of Pharmacy, Amravati.
[2]Department of Pharmaceutis, Vidyabharati College of Pharmacy, Camp, Amravati, Maharashtra, India.

***Corresponding Author: Suraj Yadav**
Dr. Rajendra Gode College of Pharmacy, Amravati.
DOI: https://doi.org/10.17605/OSF.IO/BK9JP

Article Received on 01/11/2020 **Article Revised on 21/11/2020** **Article Accepted on 11/12/2020**

ABSTRACT
Chewing Gums are mobile Drug Delivery Systems, with a potential for administering drugs either for local or systemic absorption via buccal route. It can be administered discreetly without water. Medicated Chewing Gums contains gum base along with Antiemetic agent which is intended to chew not to be swallowed. Also this formulation contains Polyisobutylene, Soya lecithin, Calcium Carbonate and Flavoring agents. The Medicated Chewing Gums were prepared by the direct compression method. The prepared formulations were evaluated for various pre-compression and post compression parameters. The *in-vitro* drug release of Formulation MCG3 showed satisfactory drug release within 30 min. at various chewing conditions. From the results it is concluded that the Chewing Gum Containing Ondansetran HCl will be the potential dosage form for the treatment of chemotherapy induced nausea and vomiting.

KEYWORDS: Medicated Chewing Gum, Ondansetron Hydrochloride, Buccal Route, Nausea And Vomiting.

INTRODUCTION
Medicated Chewing Gum (MCG) is a novel drug delivery system containing masticatory gum base with pharmacologically active ingredient and intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa. MCG is considered as vehicle or a drug delivery system to administer active principles that can improve health and nutrition. MCG represents the newest system with potential uses in pharmaceuticals, over the counter medicines and nutraceuticals.[1] The drugs intended to act in oral cavity often have low water/saliva solubility and chewing gum constitute a valuable delivery system for such drugs. Medicated chewing gum is a solid or semisolid dosage form which consists of one or more active ingredient (water soluble or insoluble) incorporated in water insoluble base. Many scientific studies have explored the role of chewing gum in promoting healthy teeth. Gum chewing is a common habit in many countries.[2] Most of the drug released from the gum through mastication is rapidly absorbed via the buccal cavity due to its large vascularization; therefore, a faster absorption results in a shorter duration of action.[3] The oral mucosa is highly perfused with blood vessels having a blood flow of 20 – 30 ml/ min for each 100g of tissue.[1-4] Drugs absorbed via the buccal cavity have direct access to the systemic circulation which bypasses intestinal and hepatic first-pass metabolism, thus potentially increasing their extent of absorption.[14.15]

Ondansetron HCl is used as drug because it exhibits half life of 5 hrs. It is sparingly soluble in water. Absorption through oral cavity is good.[5-11] It is majorly used in treatment of chemotherapy induced nausea and vomiting.

History of Medicated Chewing Gum
One thousand years ago, the Mayan Indians chewed tree resin from the sapodilla tree in order to clean their teeth and freshen the breath.[6,7] Shortage of natural gum bases during World War II enhanced development of the synthetic gum bases that are used today. The first patent for the production of chewing gum was filed in 1869 and was issued to Mr. W. F. Semple in Ohio under U.S. Patent No. 98,304. The first medical chewing gum, AspergumR, was launched in 19288,9. This chewing gum contains the analgesic substance acetylsalicylic acid known from AspirinR tablets. Chewing gum did not gain acceptance as a reliable drug delivery system until 1978, when nicotine chewing gum became available. Another commercially available medical chewing gum is dimenhydrinate-containing chewing gum for motion sickness.

Chewing gum has an old and long history, in 50 AD; the Greeks sweetened their breath and cleansed their teeth by

using mastiche, a resin from the bark of mastic tree. (The English word "masticate" is derived from the root word mastiche) At the beginning of its history this product was not so much accepted by the public. Spruce gum, which was manufactured in 1848, became the first chewing gum product to be manufactured commercially Called "STATE OF MAINEPURE SPRUCE GUM." However, its use was eventually replaced by paraffin, which is still being chewed in some areas.

MATERIALS AND METHODS

Ondansetron HCL obtained from Dev life Corporation Mumbai, India. Polyisobutylene, Soya oil and Lecithin were obtained from Univenture Pvt. Nagpur, bees Wax, Paraffin Wax, calcium carbonate; Ethanol, Methanol and other reagent were of analytical grade.

Formulation by Direct Compression Method

Polyisobutylene, Soya-Lecithin, beeswax, Paraffin Wax, calcium carbonate, Mannitol, Peppermint and Ondansetran Hcl are weighed separately and mixed in ascending order in a mortar. After mixing, ingredients thoroughly grounded in a mortar pestle and then required quantity of Glycerol was added. Then the whole mixture was mixed and ground thoroughly using a pestle mortar. After mixing and grinding the mixture was subjected for compression by using rotary tablet press compression machine to form medicated chewing gum as shown in Table no1.

Table no. 1: Formulation table of Ondansetran Hcl Medicated Chewing Gum.

Ingredients	MCG1	MCG2	MCG3	MCG4	MCG5	MCG6	MCG7	MCG8	MCG9
Ondansetran Hcl	5	5	5	5	5	5	5	5	5
Paraffin wax	10	20	30	40	50	20	20	20	20
Polyisobutylene	10	10	10	10	10	7	8	9	10
Calcium Carbonate	30	30	20	22	15	35	25	20	30
Glycerol	8	7	8	4	5	10	15	10	7
Soya	8	4	7	4	6	4	7	7	4
Lecithin	15	15	10	7	5	15	10	23	20
Orange	3.5	3	3	3	4	3	4	3	3
Strawberry	9	5	6	4	4	5	7	5	4
Dye	1	1	1	1	1	1	1	1	1

Evaluation

Evaluation of flow property of mixture

Bulk density and tapped density

Directly compressible blend was poured gently through a glass funnel into a graduated cylinder of bulk density apparatus. Then Bulk density and tapped density were calculated.

$$\text{Bulk density} = \frac{\text{Weight of sample in gram}}{\text{Final volume of sample contained in cylinder}}$$

$$\text{Tapped density} = \frac{\text{Weight of sample in gram}}{\text{Final volume after tapping in cylinder}}$$

Carr's compressibility index

Used for compare the bulk density and tapped density.
The Compressibility index was calculated by the formula

$$\text{Carr's index} = \frac{\text{Tapped Density - Bulk Density}}{\text{Tapped density}}$$

Hausner ratio

The flow properties of blend, granules or Powder are measured by this ratio.

$$\text{Hausner ratio} = \frac{\text{Bulk Density}}{\text{Tapped Density}}$$

Drug Excipients Interaction Study

Fourier Transform Infrared Spectroscopy (FT-IR)

It was determined by FT-IR (Shimadzu). The base line correction was done with blank background measurement. Then the spectrum of dried drug was run. FT-IR spectra were recorded in the wavelength region of 4000 to 500 cm^{-1}.
Peak 1: pure Ondansetron Hcl
Peak 2: Ondansetron Hcl + Polyisobutylene
Peak 3: Ondansetron Hcl + Other All Excipients
Peak Observed at: 3100-3200 cm^{-1}

Differential scanning calorimetry of ondancetron HCl

Differential Scanning calorimetry study was performed by using Shimadzu DSC-60 (Japan) instrument. The DSC thermogram of ondancetron HCL were generated and investigated for presence of peaks. The temperature range was taken from 30°c to 300°c.
Melting point: 231-232°C
Onset : 204°C
End: 215°C
Peak: 211°C

Morphology of Formulation

Medicated Chewing Gums were evaluated for Its Morphological characteristics like Shape, Size and Color.

Weight Variation

Chewing gums were selected at random and the average weight was calculated. The batch passes the test if not more than two of the individual chewing gums weight deviates from the average weight by more than the acceptable percentage

Thickness

Five Chewing Gums were selected at random from individual formulations and thickness was measured by using Digital Vernier calliper scale.

Friability (%F)

Twenty Chewing Gums from each batch were selected randomly and weighed. Then put 20 tablets in Roche Friabilator for 100 revolutions. Tablets were removed, de-dusted and weighed again.

% F = (Wi-Wr/Wi) 100

Drug Content

Chewing Gums were weighed individually and powdered. An amount equivalent to 10 mg of Ondansetran Hcl was accurately weighed and placed in a 100 ml volumetric flask to prepare a 100 ppm solution in phosphate buffer pH. 6.8. From this 1ml dilute to 10 ml volumetric flask (10 ppm). The sample was measured at λmax 248 nm using a Shimadzu UV-Visible spectrophotometer and Ondansetran Hcl concentration complies with the test if the individual content is between 85% and 115% of the average content.

***In-vitro* Drug Release study**

In-vitro drug release study was performed on modified dissolution apparatus by taking a medicated chewing gum in the receptor compartment and then it was subjected for a number of compression cycle of 40 to 50 times per minute**.** Then aliquot was collected at a regular interval of 5 minutes for 30 minutes. Then drug concentration was determined by UV spectroscopy.

RESULTS AND DISCUSSION

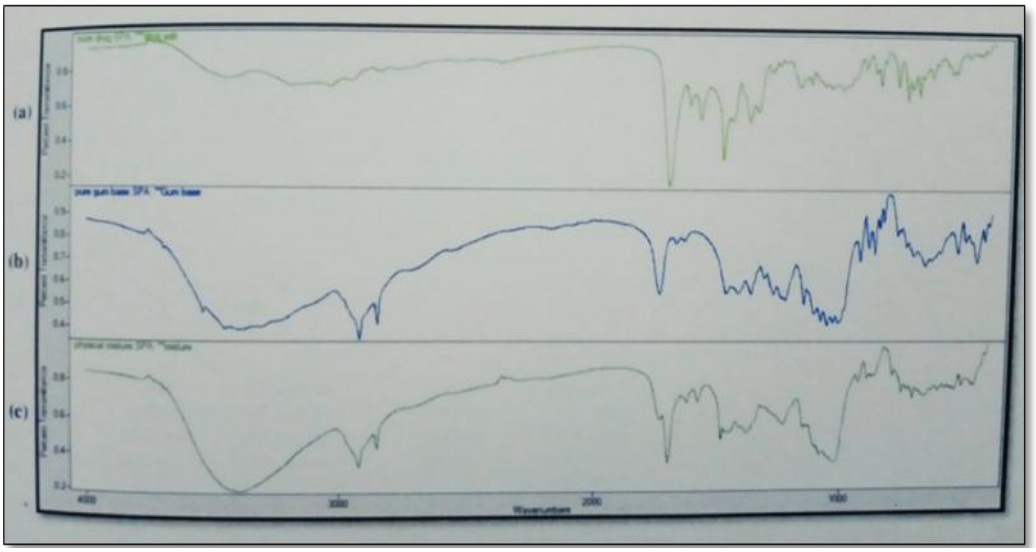

Fig:1. FTIR Spectrum.

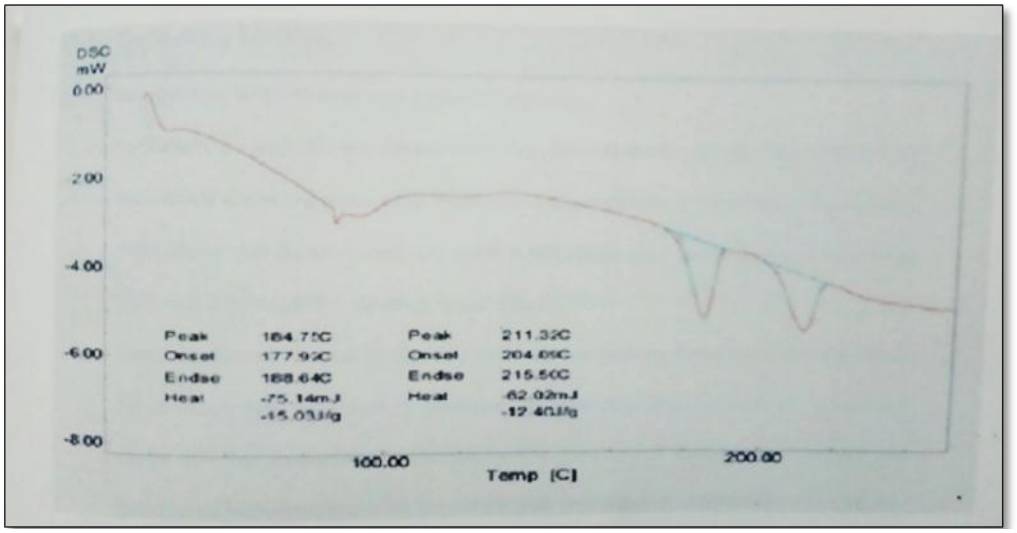

Fig.2. Differential Scanning Colorimetry.

Table: Evaluation of Prepared Medicated Chewing Gum.

Parameters	MCG1	MCG2	MCG3	MCG4	MCG5	MCG6	MCG7	MCG8	MCG9
Weight variation (gm)	1.004	1.007	1.006	1.004	1.005	1.002	1.002	1	1.002
Thickness(mm)	6.67	6.62	6.6	6.65	6.68	6.62	6.7	6.7	6.8
Content Uniformity (%)	98.2	98.26	98.37	98.06	98.56	98.45	98.82	98.05	97.51
Drug content (%)	98.5	98.01	99.26	98.4	98.82	99	98.11	98.16	98.3
% Drug Release	68.56	84.63	98.58	50.12	70.19	78.52	49.35	59.53	63.85

Table: Calibration curve of Ondansetron hydrochloride in phosphate buffer pH6.8.

Sr. No.	Concentration in µg/ml	Absorbance
1	0	0
2	2	0.102
3	4	0.217
4	6	0.385
5	8	0.492
6	10	0.712

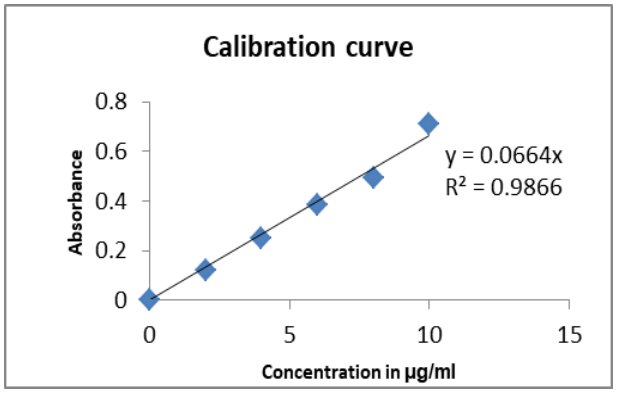

Fig: 3 calibration curve of Ondansetron Hydrochloride.

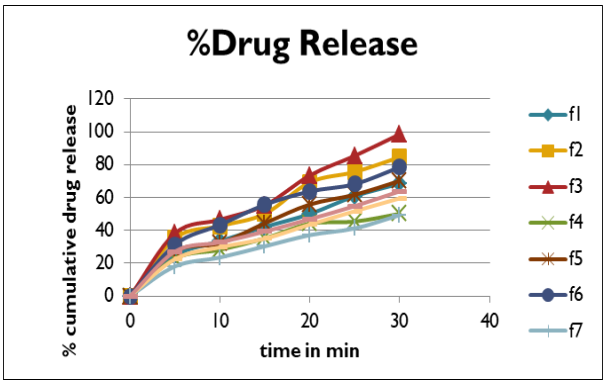

Fig: 4 Cumulative % Drug release medicated chewing gum.

CONCLUSION

The aim of this study was to explore the feasibility of Fast Dissolving Medicated Chewing Gum of Ondansetron Hydrochloride for the treatment of chemotherapy induced nausea and vomiting. A satisfactory attempt was made to develop medicated chewing gum of Ondansetron Hydrochloride and evaluated. As per the finding from current research work, it was concluded that, it provides better release of drug. As per the experimental result revealed, formulation F3 was selected as optimized formulations as they were meet the satisfactory performance. Hence, it can be concluded that medicated chewing gum of Ondansetron Hydrochloride may be providing a better

pharmacological effect, thus can be effectively used in chemotherapy induced nausea and vomiting.

Conflicts of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

ACKNOWLEDGEMENT

The authors wish to thanks to Dev life Corporation Mumbai, India for providing drug, thanks to Department of Pharmaceutics, Vidyabharati College of Pharmacy, Amravati, Maharashtra, India for providing all the facilities, digital journals, library and support during this work.

REFERENCES

1. Lee WW. Chewing gum as a delivery vehicle for pharmaceutical and nutraceutical substances. Pharm Tech Online, 2001; 2: 1-11.
2. Edgar W, Geddes D. Chewing gum and dental health - A review. Br Dent J, 1990; 168: 173-177.
3. C hristrup L.L., Angelo H.R., Bonde J., Kristensen F., Rasmussen S.N.: Relative bioavailability of methadone hydrochloride administered in chewing gum and tablets. Acta Pharm Nord, 1990; 2: 83–88.
4. Rindum J.L., Holmstrup P., Pedersen M., Rassing MR., Stoltze K.: Miconazole chewing gum for treatment of chronic oral candidosis. Scand J Dent Res, 1993; 101: 386–390.
5. S S Malke; S S Sidhya; A S Desai; V J Kadam. Ind Drugs, 2006; 43(3): 191-198.
6. Y Morjaria; W J Irwin; P X Barnett; R S Chan; B R Conway. DDT, 2004; 12 – 15.
7. L C Kvist; S B Andersson; J Berglund; B Wennergren; S M Fors. J Ph Biomed Ana, 2000; 4: 405–411.
8. K Ezhumalai; P Ilavarasan .Int J Ph Tech, 2011; 3: 725-744.
9. K A Ly; P Milgrom. J Ama Dent Assoc, 2008; 139: 553-563.
10. H Naik; S Gupta S.Int J Ph Res Dev, 2010; 2: 66-76.
11. Jacobsen J, Christrup LL, Jensen NH. Medicated chewing gum. Am J Drug Deliv, 2004; 2: 75-88.
12. Cloys L, Christen A, Christen J. The development & history of chewing gum.
13. Bulletin of the History of Dentistry, 1992; 40: 57-65.
14. Owens, L. Gumtech to Produce Aspergum and Chooz for Schering- Plough Health Care Products. Business Wire, 1998.
15. Khanekar P, Mhatre S, Momin M. Medicated Chewing Gum: A Potential Drug Delivery System. IJPFR, 2012; 2(4): 64-75.