Research Article

Formulation and Evaluation of Herbal Antimicrobial Chewing Gum Containing Neem Extract

AM. Chanale* and RP. Mishra

Department Of Quality Assurance Techniques, PDVVPF'S College of Pharmacy, Ahmednagar, Maharashtra, India-414 111.

ABSTRACT

Nowadays, due to emerging development in the oral drug delivery systems several sophisticated technologies came out. Oral route of administration has grabbed much more attention because of its convinient administration .There are various dosage forms that can be administered orally. Among which chewing gum is most popular. It is potentially useful means of administering drugs locally. In recent decades chewing gum has gained increasing acceptance as a drug delivery system. Neem is antimicrobial agent used for management of tooth decay. In mouth, Neem gets readily adsorbed to negatively charged area, including mucosa and pellicle coated teeth. In the given formulation chewing gum released the active ingredients into saliva upto the time as the gum product is masticated. In present work of Herbal chewing gum formulations were herbal food graded gum base and by using different excipients such as Honey, Sugar, Colouring and flavouring agent.

Keywords: Herbal Chewing Gum, Neem (Nimbidin), Antimicrobial Activity, Buccal Cavity.

1. INTRODUCTION

Drug can be administered via different routes of administration to produce a systemic pharmacological effect. The most common method to administer drug is oral route, in which the drug is swallowed and it enters the systemic circulation. There are various dosage form that can be administered orally. Out of which, chewing gum is most popular. It is a potentially useful means of administering drugs locally and systemically. Chewing gum has been used for centuries to clean the mouth as well as breath. In the present work non toxic natural food graded gum base has been used in the formulation of herbal chewing gum (HCG) containing antimicrobial agent Neem (Nimbidin). The aim of this work was to formulate, prepare and evaluate herbal antimicrobial chewing gum of Neem extract. Different excipients such as Honey, Sugar, Colouring and flavouring agents were used for the preparation.

2. MATERIALS AND METHODS

Neem (Nimbidin) was obtained from *PDVVPF's college of Pharmacy, vilad ghat, ahmednagar.* Natural food graded gum base was procured from Rajesh chemicals, Mumbai. Honey from Patanjali Ayurvedic store, Ahmednagar.

3. Preparation of herbal chewing gum

All ingredients were weighed accurately as shown in formulation table 1. Molten mass of natural food graded gum base was prepared and Honey was mixed thoroughly in porecelain dish. The dish was kept on water bath and temperature was maintained at about 35-45 ^{0}C. Drug Neem (Nimbidin) was then added to above mass. Corresponding amount of sugar, colouring and flavouring agent was added to above mixture with continuous stirring up to 30 min. Finally the adequate amount of flavour was incorporated in the mixture. The mass was poured into the mould and was allowed to cool at room temperature. The gum pieces were removed.

Table 1: Formulation of herbal chewing gum

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Natural food graded gum base	2 gm	2 gm	2 gm	2 gm	2 gm	2 gm	2 gm	2 gm	2 gm
Neem(Nimbidin)	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg
Honey	1.5 gm	1.0 gm	0.5 gm	1.5 gm	1.0 gm	0.5 gm	-	-	-
Sugar	-	-	-	0.5 gm	1.0 gm	1.5 gm	0.5 gm	1.0 gm	1.5 gm
Liquid Glucose	0.5 gm	1.0 gm	0.5 gm	-	-	-	1.5 gm	1.0 gm	0.5 gm
Colouring and Flavouring agent	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s	q. s

*Quantities per chewing gum

4. Physical evaluation of drug and natural food graded gum base

i. Preliminary studies

UV studies of Neem(Nimbidin) were performed using UV-visible spectrophotometer double beam (Jasco-V-630). The chewing gum base was evaluated for colour, softening range, solubility studies in different solvent. Stability studies were performed.

ii. Physical evaluation of herbal chewing gum

The formulated chewing gum were evaluated for Plasticity/Hardness.

5. RESULTS AND DISCUSSION

5.1. UV spectroscopy

λ_{max} of Neem(Nimbidin) was found to be 280nm in artificial saliva solution having pH 6.4.

Table 2: UV Absorbance V/S Conc

Conc. (µg/ml)	Abs.
0	0
2	0.0717
4	0.1445
6	0.2165
8	0.3036
10	0.3468

Calibration curve of Neem(Nimbidin)

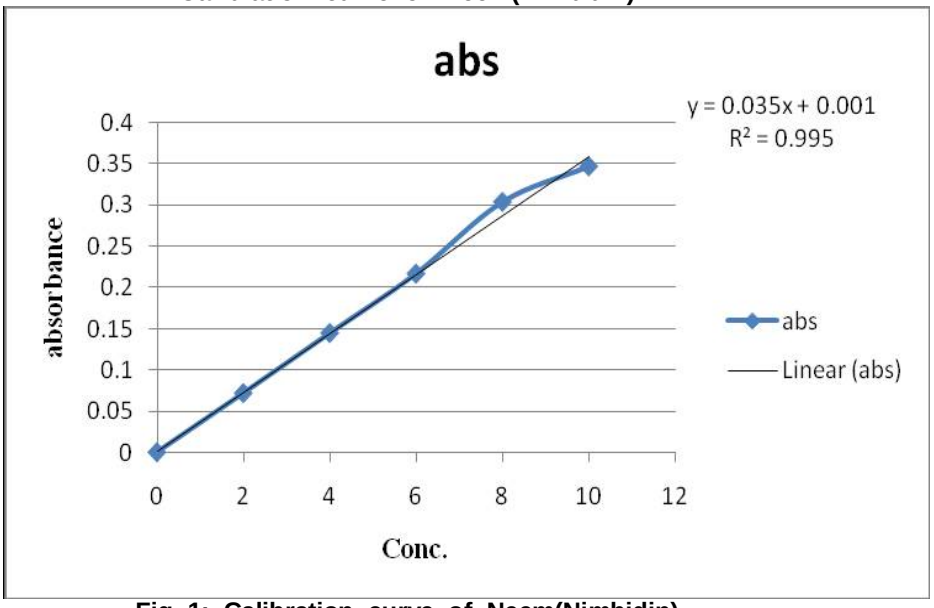

Fig. 1: Calibration curve of Neem(Nimbidin)

5.2. Physical evaluation of gum base

5.2.1. Colour

Colour of Natural food graded gum base is pale yellow.

5.2.2. Softening point

Softening point of Natural food graded gum base was observed by heating the base in petri dish. The temperature at which it starts melting is the softening point of that base. It was found to be 55-60 ^{0}C.

5.2.3. Solubility studies of Natural food graded gum base

Table 3: Solubility studies

S.No.	Solvent	Solubility(gm)/10ml
1	Alcohol	Up to 2 gm
2	Chloroform	Up to 17 gm
3	Acetone	Soluble
4	Water	Insoluble
5	Artificial Saliva	0.01 gm
6	Diethyl ether	Up to 1.2 gm
7	Phosphate buffer	0.01 gm

As the gum has showed very neglible solubility in artificial saliva and phosphate buffer, it can be concluded that the procured Natural food graded gum base was the best for use as the base herbal chewing gum preparation.

5.3. Physical evaluation of herbal chewing gum

The formulated herbal chewing gum was evaluated physically for following parameters and are mentioned in Table 4.

5.3.1. Colour

The colour of herbal chewing gum formulation was observed Visually and all the batches were light yellow in colour which was acceptable.

5.3.2. Stickiness

The formulated herbal chewing gum was placed on plain surface. A mass of 250gm was hammered on it upto 10 min. The frequency of hammering was about 30/min. None of the batch stuck to hammer or surface.

5.3.4. Weight variation

Chewing gum from each batch were individually weighed on analytical balance, the average weight and standard deviation were calculated which was found in acceptable limit.

5.3.5. Plasticity/Hardness

Hardness of chewing gum was determined by Monsanto hardness tester and the average hardness and standard deviation were reported.

5.3.6. Percentage drug content

% Drug content of formulated chewing gum was determined by weighing 4000mg chewing gum equivalent to 10mg Neem(Nimbidin) and transferring into volumetric flask. About 60ml of artificial saliva was added, sonicated for 10 min, then shaken by mechanical means for 30 min and volume was adjusted to 100ml with the same solvent. Again it was sonicated and filtered. Percentage drug content was determined spectrophotometrically at 280nm. Same procedure was repeated for three times.

Table 4: Physical evaluation of herbal chewing gum

S.No.	Batch	Stickiness	Colour	Weight variation(mg)	Hardness Kg/cm^2	% Drug content
1	F1	Non sticky	Light Brown	4000±0.014	2±0.1	84.36%
2	F2	Non sticky	Light Brown	4000±0.009	2.5±0.1	90.96%
3	F3	Non sticky	Light Brown	4000±0.017	2.5±0.1	84.93%
4	F5	Non sticky	Light Brown	4000±0.015	2.5±0.2	93.07%
5	**F5**	**Non sticky**	**Light Brown**	**4000±0.054**	**2.5±0.15**	**96.31%**
6	F6	Non sticky	Light Brown	4000±0.006	2.5±0.1	89.47%
7	F7	Non sticky	Light Brown	4000±0.005	2.5±0.12	89.17%
8	F8	Non sticky	Light Brown	4000±0.007	2.5±0.1	91.76%
9	F9	Non sticky	Light Brown	1000±0.005	2.5±0.1	85.43%

5.3.7. In vitro dissolution studies

In order to study the in vitro dissolution pattern from chewing gum, it was necessary to design an apparatus, which could give same impact of mastication on herbal chewing gum. This was necessary in order to mimic the human mastication. After an extensive literature survey it was decided to modify the disintegration test apparatus and fabricate suitable chewing gum apparatus.

Figure 2: Lab fabricated herbal chewing gum apparatus with S.S die and punch. Release measurements were performed using lab fabricated herbal chewing gum test apparatus at 50 rpm. In each flask a 900ml of artificial saliva pH 6.4 was filled. The temperature was maintained at 37 ^{0}C. At predetermined interval (0, 2, 4, 6, 8, 10, 12 and 14)(min) absorbance was recorded spectrophotometrically at 280nm and the percentage of drug released was determined as a function of time

Table 5: Cumulative % drug release

S.No.	Time (Min)	% Cumulative Drug Release								
		F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2	2	4.14	3.96	25.94	30.38	48.20	36.31	38.11	42.54	31.957
3	4	26.25	32.06	39.31	42.41	56.90	61.66	63.96	62.34	45.77
4	6	31.5	51.48	55.62	63.79	66.29	59.22	63.68	64.86	67.80
5	8	37.92	55.54	72.72	74.90	73.42	64.56	68.94	71.80	71.51
6	10	45.48	62.56	75.31	80.40	85.45	66.03	70.72	74.97	78.39
7	12	52.17	69.94	77.86	91.36	92.35	70.25	75.08	78.15	85.40
8	14	60.09	71.97	79.97	96.45	98.43	86.09	88.95	89.49	92.00

Table 6: % Drug release of optimized formulation (Batch F5)

S.No.	Time (min)	Avg. % Drug Release	Amt. (mg)
1	0	0.000	0.00
2	2	48.203	7.23
3	4	56.902	8.54
4	6	66.295	9.94
5	8	73.421	11.01
6	10	85.453	12.82
7	12	92.351	13.85
8	14	98.432	14.76

5.3.8. Stability studies of natural food graded gum base

The batch F5 has shown maximum drug content and all acceptable parameters as compared to others batches and also maximum percentage cumulative drug release, stability studies were performed for the optimized batch F5. In the stability studies, stability of gum was checked by keeping formulation at different conditions as per ICH guidelines viz. at 40^0C± 20^0C /75% RH ±5% RH for one month in stability chamber.

Table 7: Stability studies of optimized batch F5

S.No.	Properties	Observation
1	Colour(Initial)	Pale yellow
2	Colour(After one month)	Pale yellow
3	Softening point (Initial)	55.0 ^{0}C - 60.0 ^{0}C
4	Softening point (After one month)	55.0 ^{0}C - 60.0 ^{0}C
5	% Drug Content	98.43%

CONCLUSION

The present work was aimed to develop the herbal chewing gum as drug delivery system for Neem(Nimbidin) having antimicrobial activity. Chewing gum formulations were prepared using Natural food graded gum base, Honey, sugar, colouring and flavouring agent. Herbal chewing gum formulations were evaluated for different parameters like stickiness, weight variation, percent drug content and in vitro drug release test were performed. In-vitro release test was performed using lab fabricated herbal chewing gum apparatus. The disintegration test apparatus was modified in such a way that the formulation was pressed continuously like mastication process. From the in vitro drug release data it was concluded that drug release from the herbal chewing gum was satisfactory. Percent drug release of all formulation batches is in between 84.38% to 96.45%. Batch F5 containing Honey was found to be best formulation in all aspect.

ACKNOWLEDGEMENT

Authors are thankful to PDVVPF's college of pharmacy, Ahmednagar for providing all the facilities for completion of this research work. Authors are also thankful to Rajesh chemicals, Mumbai for providing Natural gum base.

REFERENCES

1. Mohan AU, Suraj RW and Abhishek DD. hebal chewing gum: Modern approach to mucosal drug delivery system. Asian J Res Pharm science. 2012;2(4):150-159.
2. Sabera K and Sutradhar K. Synthetic chewing gum: An unconventional drug delivery system, International Current Pharmaceutical Journal. 2012;1(4):86-91.
3. May MS and Magda AE. Design and evaluation of Mucoadhesive buccal patches for local delivery of Chlorohexidin Di. International Journal of Drug Formulation and Research. 2012; 3(4):89-107.
4. Thomas I. Chlorohexidin containing chewing gum, Schweiz Monatsschr Zahmed. 2006; 116(5):476-483.
5. Ranjan M and Vishaka G. Comparison of the effectiveness of a commercially available synthetic mouthrinse with chlorohexidin at the clinical and patient level, Journal of Indian Society of Periodontology. 2014;15(4):349-52.

6. Farhad M and Piyush T. Formulation and texture characterization of synthetic chewing gum delivery of Dimenhydrinate Hydrochloride, Derpharmacia Lettre. 2011;3(6):179-192.
7. Swamy NGN and Shilpa P. Formulation and characterisation of synthetic chewing gum of Dextromethorphan Hydrobromide, Indian drugs. 2012;49(12):29-35.
8. Shivanand P, Manish G and Viral D. Development, In-vitro Evaluation and Physical characterisation of synthetic chewing gum: Chlorohexidine. Der Pharmacia Lettre. 2009; 1(2): 286-2.
9. Pandey S, Goyani M and Devmurari V. Development, In-Vitro Evaluation and characterization of Medicated Chewing Gum: Chlorhexidine Gluconate. Der Phamacia Lettre. 2009;1(2):286-292.
10. Jain H, Shah M and Shah B. Medicated Chewing Gum: A Novel Oral Drug Delivery. Int J Drug Formulation Res. 2010;1(3):80-96.
11. Girish K and Bhat SS. Neem - A Green Treasure. Electronic Journal of Biology. 2008; 4(3):102-111.
12. Pant N, Garg HS and Madhusudanan. Sulfurous Compounds from Azadirachta indica leaves. 1986;57:302-304.
13. Khosla P, Bhanwra S and Singh J. A Study of hyoglycaemic effects of Azadirachta Indica(Neem) in normal and alloxan diabetic rabbits. Indian J Physiol Pharmacol. 2000; 44:69-74.
14. Rahman MF, Siddiqui MK and Jamil K. Effects of Vepacide(Azadirachta Indica) on asartate and alanine aminotransferase profiles in a subchronic study with rats. Hum Exp Toxicol. 2001;20:243-249.
15. Pai MR, Acharya LD and Udupa N. The effect of two different dental gels and a mouthwash on plaque and gingival scores. A six week clinical study. Int Dent J. 2004; 54:219-23.
16. Gandhi S, Singh R and Kaur R. Acute toxicity study of the oil from Azadirachta Indica seed (neem oil). Journal of Ethnopharmacology. 1988;23:39-51.