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Formulation and Evaluation of Medicated Chewing Gums of Chlorpheniramine Maleate

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ABSTRACT

The aim of the present work is development and evaluation of Chlorpheniramine maleate medicated chewing gums and to study the influence of different plasticizers on physicochemical parameters and *in vitro* drug release profile. Chlorpheniramine maleate is used to relieve symptoms of allergy, hay fever and common cold. Prepared formulations are evaluated for thickness, hardness, weight variation, friability, drug content and drug-excipient interactions. *In vitro* drug release was performed by modified dissolution apparatus. Better consistency of formulation and faster release of drug was obtained with glycerol (F6) & castor oil (F12). In all formulations, when concentration of plasticizers increases, increased drug release is observed. The formulations prepared with glycerol as a plasticizer i.e., F6 shows good drug release compared to formulations prepared with castor oil.

INTRODUCTION

Oral route is the most preferred route amongst the patient and clinicians due to various advantages it offers. Man has a habit of chewing the chewing gum since ancient times. Today it is one of the most popular dosage form, used for delivering the many active components [1]. Medicated chewing gum is solid, single-dose preparations that have to be chewed and not swallowed; chewing gums contain one or more active ingredient that is released by chewing [2,3]. Medicated chewing gum offers a highly convenient patient–compliant way of dosing medications, not only for special population groups with swallowing difficulties such as children and the elderly but also for the general population including the young generation.

Various excipients used in the manufacture of chewing gums like elastomers, elastomer solvents, bulking agents, softening agents, sweetening agents, flavouring agents, antioxidants, glidants [4,5,6]. Medicated chewing gums are prepared by different methods like conventional/traditional method, cooling and grinding method and direct compression method [7, 8].

Chlorpheniramine maleate is used to relieve symptoms of allergy, hay fever and common cold. It has poor oral bioavailability as it undergoes extensive first pass hepatic metabolism [9]. So it is a suitable candidate prepare into a medicated chewing gum. In this work, medicated chewing gum of chlorpheniramine maleate was prepared by direct compression method using different concentrations of plasticizers like glycerol and castor oil.

MATERIALS AND METHODS

Chlorpheniramine maleate was received as a gift sample from Meditab Ltd., India, Polyvinylpyrrolidone obtained from Bliss chemical & pharmaceuticals India Ltd.(Thane). Plasticizers and all other ingredients are obtained from S.D. Fine Chem. Ltd., Mumbai.

Drug-Excipient Compatability Studies:

FT-IR Studies: The drug- excipient compatibility study was carried out by FTIR (Bruker Alpha E Opus), FTIR spectra of pure drug and optimized formulation were recorded. The baseline correction was done by blank background and 400-4000 cm^{-1} was used as scanning range.

Standard Graph for Chlorpheniramine maleate: 100 mg of drug was taken and placed in 100 ml of volumetric flask, 6.8 pH phosphate buffer was used to made the volume to 100 ml, which is equal to 1000 µg/ml, by using this stock solution prepare different dilutions from 10-50 µg/ml and the absorbance was recorded at 265 nm using U.V spectrophotometer.

Preparation of chewing gum by direct compression method:

Required quantities of drug, PVP, $CaCo_3$ are taken into mortar and mixed. To this melted beeswax and plasticizers were added and mixed well. To this mixture remaining ingredients are added and compressed by using Rotary Tablet Compression Machine (Cadmach, Ahmedabad, India).

Formulation Chart:

Table 1: Formulae of Chlorpheniramine maleate medicated chewing gums with different concentrations of plasticizers

Formulation Code	CPM (mg)	Bees Wax (mg)	Glycerol (mg)	Castor oil (mg)	Dextrose (mg)	$CaCO_3$ (mg)	PVP (mg)	Mannitol (mg)	Flavour (mg)	Mg. stearate (mg)	Aerosil (mg)
F1	5	20	5	-	24	24	10	200	3	1	3
F2	5	20	10	-	24	24	10	200	3	1	3
F3	5	20	15	-	24	24	10	200	3	1	3
F4	5	20	20	-	24	24	10	200	3	1	3
F5	5	20	25	-	24	24	10	200	3	1	3
F6	5	20	30	-	24	24	10	200	3	1	3
F7	5	20	-	5	24	24	10	200	3	1	3
F8	5	20	-	10	24	24	10	200	3	1	3
F9	5	20	-	15	24	24	10	200	3	1	3
F10	5	20	-	20	24	24	10	200	3	1	3
F11	5	20	-	25	24	24	10	200	3	1	3
F12	5	20	-	30	24	24	10	200	3	1	3

Total Weight of each chewing gum: 300mg

Precompression study:

The blend which is made into chewing gum by direct compression method was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose.

Evaluation Studies:

Medicated chewing gums are evaluated for hardness, weight variation, thickness, friability, drug content and *in vitro* drug release studies.

Hardness: Due to absence of any reported method, it was decided to use the Monsanto type hardness tester for determination of hardness of all MCG formulations. The average values, standard deviation and relative standard deviation were calculated.

Weight variation: According to specifications weight of 20 chewing gums are taken then average weight is calculated from that standard deviation is calculated.

Drug Content: Randomly 10 medicated chewing gums were taken, crushed and amount equivalent to 5 mg of drug was taken and dissolved in 6.8 pH phosphate buffer, sonicated, filter the solution and record the absorbance using spectrophotometer at 265nm. Then, drug concentration was measured using standard graph. The measurements were carried out in replicates (n=6).

***In vitro* drug release studies:** After extensive literature survey, disintegration apparatus was slightly modified for this study. The modified apparatus which mimics the human chewing behavior was used to determine the drug release. The MCG placed in 500 ml of 6.8 pH phosphate buffer and samples were collected periodically for each time interval of 5, 10, 15, 20, 25 and 30 min and absorbance was measured at 265nm. Measurements were carried out in replicates (n=6) and mean ±SD values are recorded.

RESULTS AND DISCUSSION

Drug – excipient compatibility studies:

FT-IR Studies: The FT-IR spectrum of pure drug and optimized formulations were shown in Fig.1 & 2. FT-IR spectra results showed that same peaks were observed for pure drug and optimized formulation and there are no additional peaks are observed. Therefore, from FT-IR spectra, it could be concluded that there is no incompatibility between drug and excipients.

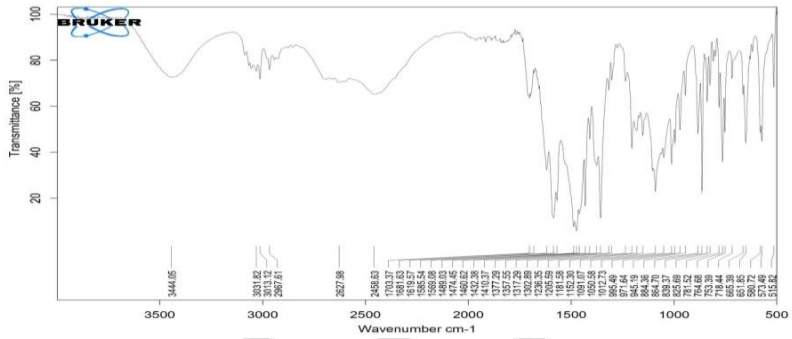

Figure 1: FTIR of Pure Drug

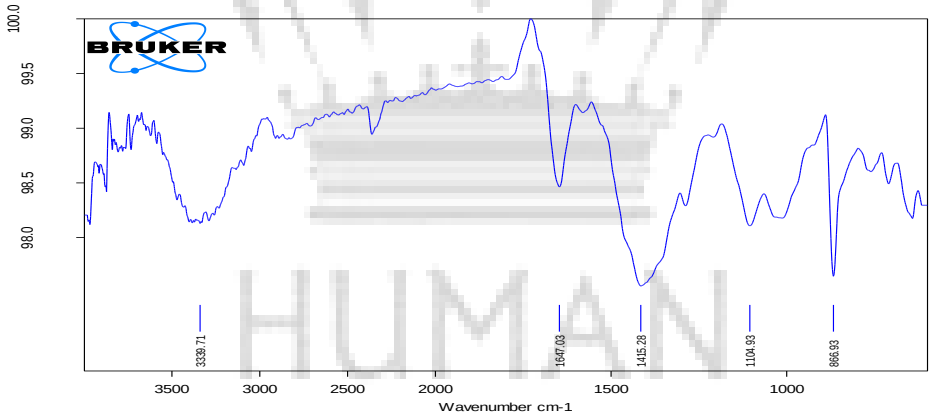

Figure 2: FTIR of Optimized formulation

Table 2: Calibration Curve of Chlorpheniramine Maleate in 6.8 pH Phosphate Buffer

Concentration (µg/ml)	Absorbance
10	0.188±0.001
20	0.318±0.004
30	0.479±0.001
40	0.637±0.003
50	0.780±0.002

Precompression Evaluation of the Powder Blend:

The powder blend is evaluated for different parameters and bulk density values are found to be 0.312-0.323, tapped density values are 0.332-0.358, % compressibility values are 5.12-10.33, angle of repose values 26°16′ -28°38′. All the reported values are within standards, it means all the powder blends have good flow properties.

Table 3: Post-Compression Parameters of Chlorpheniramine Maleate

Formulation Code	Hardness (kg/cm^2)	Thickness (mm)	Weight variation (mg)	Friability (%)	Drug content (%)
F1	3.5 ±0.44	4.08±0.17	299.8±1.48	0.36±0.08	96.12±0.12
F2	3.6±0.31	3.40±0.25	300.4±0.54	0.39±0.12	96.51±0.11
F3	3.5±0.40	3.21±0.80	298.6±0.41	0.43±0.31	94.65±0.13
F4	3.9±0.15	4.2±0.20	300.8±1.64	0.12±0.22	97.34±0.23
F5	3.5±0.27	4.08±0.66	305.6±1.14	0.54±0.16	98.35±0.22
F6	3.5±0.30	3.31±0.25	299.2±0.83	0.58±0.35	95.04±0.11
F7	3.5±0.57	4.1±0.71	299.9±0.67	0.64±0.41	96.32±0.13
F8	3.4±0.60	4.0±0.89	299.0±0.43	0.37±0.37	98.45±0.14
F9	3.5±0.54	4.02±0.51	300.2±0.61	0.41±0.42	97.76±0.16
F10	3.4 ±0.44	4.01±0.17	299.8±1.43	0.39±0.37	98.19±0.11
F11	3.5±0.31	3.72±0.25	300.4±0.44	0.33±0.26	97.32±0.12
F12	3.5±0.40	3.81±0.80	298.6±0.42	0.45±0.54	97.56±0.13

The prepared medicated chewing gums were evaluated for weight variation, hardness, thickness, friability, % drug content and *in vitro* drug release studies. Hardness values of prepared medicated chewing gums were in between 3.4-3.9 kg/cm^2. Weight variation values are in between 298-305 mg. Friability values were in the range of 0.12-0.64%. Drug contents values were found to be in the range of 94.65-98.45%. All evaluated parameters values are found to be within limits.

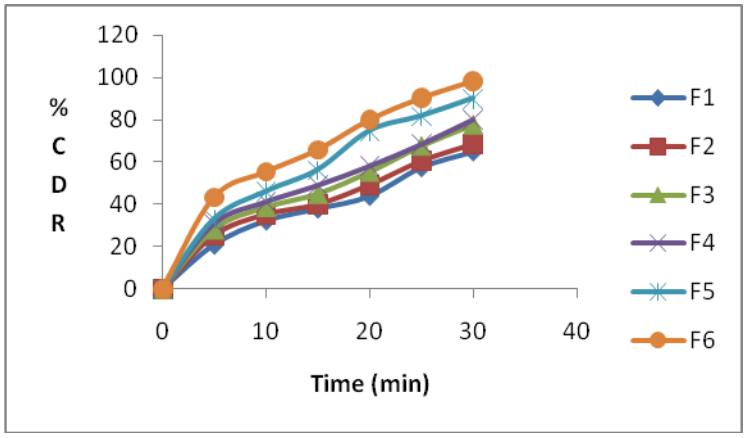

Figure 3: Cumulative drug release profile of various formulation of CPM (F1-F6)

In vitro drug release is conducted by modified dissolution apparatus. % cumulative drug release graphs showed that as the concentration of glycerol increases there is an increase in the drug release because of soft nature provided by the glycerol to the formulation. In all these formulations, F6 showed the drug release of 98.12% within 30 min. It means that maximum drug release was observed using this formulation, so it is said to be optimized formulation of F1-F6 series using glycerol as a plasticizer which is prepared by direct compression method.

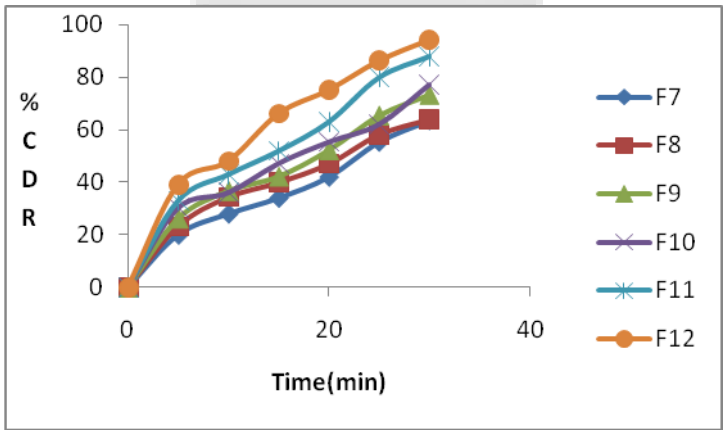

Figure 4: Cumulative drug release profile of various formulations of CPM (F7-F12)

Cumulative drug release profiles of series of formulations from F7-F12 prepared with castor oil as a plasticizer showed in Fig.No.4. F12 formulation showed highest drug release of 94.16%. From formulations F7-F12, it was observed that the concentration of castor oil increases gradually the drug release also increased. Hence, concentration of plasticizer influences

consistency of the formulation as well as drug release. It was observed that formulations prepared with glycerol and castor oil as a plasticizer both show good drug release but F6 formulation shows highest drug release which is prepared with glycerol.

Optimized formulations were kept for stability studies as per ICH guidelines at 25±2°C/60±5% RH, 40±2°C/75±5% RH. Then the stability results of best formulation after 180 days were compared with their initial results, it was found that there was no significant difference in drug content of optimized formulations.

CONCLUSION

The study reveals that amount of plasticizer used for the preparation of medicated chewing gums is the important parameter which influences the drug release and direct compression is the suitable method to prepare medicated chewing gums. Hence, it is the better option to prepare chlorpheniramine maleate into a medicated chewing gum which would be quite effective, providing quick relief from common cold.

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