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Development and *In-Vitro* Evaluation of Medicated Lollipop Containing Mebendazole for Paediatrics

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ABSTRACT

In the present investigation an attempt has been made to prepare and evaluate medicated lollipop of mebendazole. One of the major health problems faced by hundreds of millions of school-age children is infection by helminths, more commonly known as worms. Mebendazole is used as a broad-spectrum anthelmintic. The conventional dosage forms like tablets, capsules, syrups etc are inconvenient for paediatric patients because of difficult to swallow tablets and capsules or unpleasant taste of drug. As a result, the demand for developing new technologies has been increasing day by day. Lollipops or lozenges are flavored medicated dosage forms intended to be sucked and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base. Medicated lollipop is designed to improve patient compliance, acceptability and increase oral retention time. The lollipops were prepared by heating and congealing method using methylcellulose as polymer. Drug-excipient compatibility study was carried out using FT-IR. All the formulations were subjected to various physicochemical evaluations like weight variation, hardness, drug content, friability etc. The *in-vitro* dissolution study of F0 was found to be 96.14% at 15min whereas F1 was found to be 99.33% at 25min. Stability study was carried out as per ICH-Guidelines (Q1A) at 30^{o}C and 65% RH. From the present study it can be concluded that addition of hydrophilic polymers yield good result to prolong oral retention time of lollipop. Medicated lollipop can provide an attractive alternative formulation in the treatment of paediatric patients.

Keywords: Medicated lollipop, Mebendazole, methylcellulose (MC)

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INTRODUCTION

One of the major health problems faced by hundreds of millions of school-age children is infection by helminths, more commonly known as worms[1].Secondary disease manifestations due to the soil-transmitted helminths are varied ranging from malnutrition to respiratory complications. It is probable that protein energy malnutrition and iron-deficiency anemia cause severe morbidity and growth retardation among children[2].Mebendazole is a broad-spectrum anthelmintic. It causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules[3].Oral administration is the most popular route due to ease of ingestion, pain avoidance and most importantly patient compliance. Traditional tablets and capsules are inconvenient for paediatric patients because of difficult to swallow it or unpleasant taste of liquid dosage forms. Since from past decade, there has been an increased demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing day by day[4].Lozenges or lollipop are solid preparations that are intended to dissolve in mouth or pharynx. They may contain one or more medicaments in a flavoured and sweetened base and are intended to treat local irritation or infection of mouth or pharynx and may also be used for systemic drug absorption[5].It is found that sucrose based medicated hard boiled lozenges will be an alternative dosage forms for paediatric patients[6].

MATERIALS AND METHODS:

Mebendaole was obtained from Yarrow chem. Product, Mumbai. Methylcellulose, sucrose, dextrose and citric acid received from Himedia, Mumbai and raspberry flavouring agent received from classic aromatics. All other chemicals were used of analytical reagent grade.

Preparation of medicated lollipop[7, 8]:

Required quantity of sugar syrup was prepared mixing sugar and water. Dextrose was dissolved in small quantity of water and heated it to 110^{o}C till dextrose dissolves completely forming as clear viscous syrup. Then the dextrose syrup was poured into the sugar syrup and heated to 160^{o}C till the colour changes to golden yellow. Flavour was added between 120^{o}C to 135^{o}C then temperature was bought down to 90^{o}C and drug, polymer and other ingredients were added and mixed it well. The prepared mixture was poured into the calibrated mould and kept it for air dry for 1-2 hr. The prepared tablets were stored wrapped in aluminium foil and stored in desiccators to prevent moisture uptake. The final weight of each lozenge is 5gms.

Table 1: Formulation Chart

Ingredients	F0	F1	F2	F3
Mebendazole(mg)	100	100	100	100
Sucrose(mg)	3450	3425	3400	3375
Dextrose(mg)	1400	1400	1400	1400
Methylcellulose(mg)	-	25	50	75
Citric acid(mg)	50	50	50	50
Raspberry flavour	q.s	q.s	q.s	q.s
Total Weight	5gm	5gm	5gm	5gm

Drug-excipient interaction study[9]:

For studying drug-excipients interaction, prepared lozenges were subjected for FTIR studies.

Weight variation[10]:

The weight variation conducted by weighing 20 lollipops individually and calculating the average weight and comparing the individual lollipops weight to the average value.

Diameter and Thickness[9]:

Diameter and thickness of the lozenges were measured using vernier calipers. The test was performed for three lozenges and standard deviation was calculated.

Hardness[9]:

It was determined by using Pfizer tablet hardness tester. The test was performed for three lozenges and standard deviation was calculated.

Drug content[9]:

The content uniformity was tested by powdering one lozenge and dissolving the powder content in 100ml of 0.1 N HCl containing 1% SLS in a 100ml volumetric flask. From this 1ml was diluted with 0.1N HCl containing 1% SLS up to 100ml and absorbance was recorded at λ_{max}.

Friability[10]:

The friability of the lollipops determined by using Roche Friabilator. Weighed lollipops were place in the friabilator and operates for 4 min at 25 rpm. The lollipops are then made free from dust and reweighed. The percentage friability is calculated.

***In-vitro* dissolution study[9]:**

In-vitro release studies were carried using USP-II dissolution apparatus. 900ml of 0.1 N HCl containing 1% SLS at 37±0.5^{o}C is taken as dissolution media. The rpm of the paddle was fixed at 100. Samples were withdrawn at an interval of 5min up to 30min and absorbance was recorded at λ_{max}.

Stability studies[11]:

Stability studies for the lollipops were carried out at 30°C at 65%RH as per ICH-Guidelines (Q1A). For every 45days the parameters like physical appearance, weight variation, hardness, drug content and *in-vitro* dissolution studies were determined.

RESULTS AND DISCUSSION

In the present study, an attempt was made to develop medicated lollipop of mebendazole. Formulations were subjected to various parameters such as weight variation, thickness, diameter, hardness, drug content, friability and *in-vitro* dissolution study. Stability studies were performed as per ICH-Guidelines (Q1A).Figure 1 and Figure 2 shows the FT-IR spectra of pure drug and excipient which showed that there is no interaction found between drug and excipient. All the formulations showed good physical appearance. The weight variation was found to be in range of 4.92±0.06gm to 5.05±0.02gm. Thickness was found to be in the range of 7.30±0.00mm to 7.46±0.05mm whereas diameter was found to be 2.74±0.00cm which is uniform for all formulations. The results of weight variation, thickness and diameter were depicted in Table 2.

Table 2: Evaluation Parameters of Medicated Lollipop of Mebendazole

Parameters	**F0**	**F1**	**F2**	**F3**
Weight variation(gm)	4.93±0.06	4.92±0.06	5.02±0.07	5.05±0.02
Thickness(mm)	7.33±0.05	7.30±0.00	7.46±0.05	7.33±0.05
Diameter(cm)	2.74±0.00	2.74±0.00	2.74±0.00	2.74±0.00
Hardness(kg/cm^2)	10.1±0.15	10.1±0.20	10.2±0.23	11.3±0.11
% Drug content	98.20±0.85	97.23±0.35	97.66±0.47	97.80±0.26
% Friability	0.45	0.23	0.28	0.31

Hardness was found to be in the range of 10.1±0.15kg/cm^2 to 11.3±0.11kg/cm^2 whereas the percentage friability of all formulations was found to be in range of 0.23% to 0.45% which was found to be well within maximum 1% limit. The results of hardness and friability indicated that the lollipops are mechanically stable. The drug content was found to be in range of 97.23±0.35% to 98.20±0.85% which is within acceptable range as specified in Indian Pharmacopoeia (95%-105%). The results of hardness, friability and drug content showed in Table 2.

The *in-vitro* dissolution study of formulation F0 (without polymer) was found to be 96.14% at 15min. Individual formulation F1, F2 and F3 (containing 0.5%, 1% and 1.5%w/w of MC) showed the percentage cumulative drug release of 99.33% at 25min, 97.78% at 30min and 95.58% at 30min respectively. The details of *in-vitro* dissolution study showed in Table 3. The stability studies showed very slight changes in physicochemical properties and in dissolution studies. Figure 3 shows the comparison of drug release profile of all formulations. F0 (without polymer) shows quick release of drug whereas methylcellulose is a hydrophilic polymer, hence

facilitates quick release of drug. But as the concentration crosses the optimum quantity it retards drug release.

Table 3: *In-Vitro* Drug Release Data of Formulation F0 to F3

Time (min)	F0	F1	F2	F3
5	53.21	30.32	25.40	22.68
10	77.29	56.61	49.46	42.21
15	96.14	78.24	69.76	59.46
20	-	98.49	86.88	74.71
25	-	99.33	97.22	86.46
30	-	-	97.78	95.58

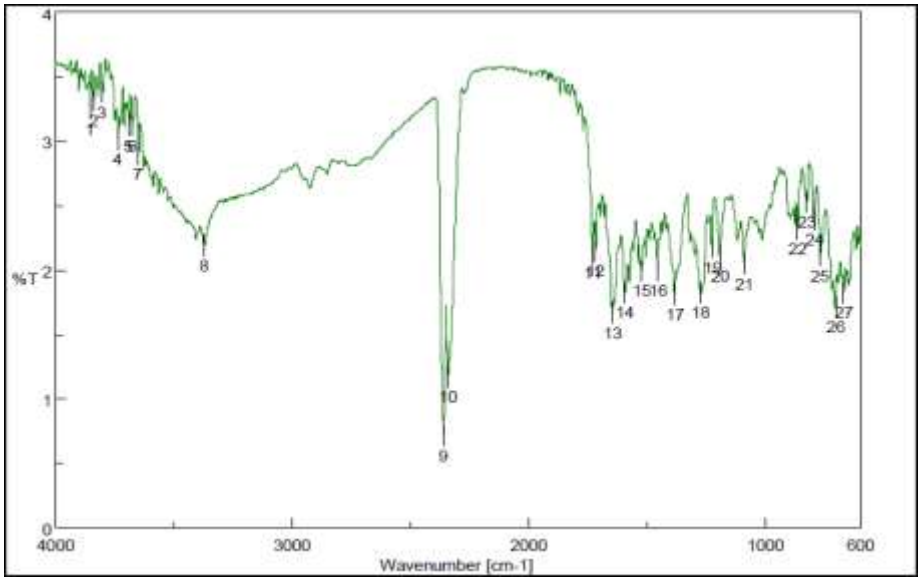

Figure 1: FTIR Spectra of Mebendazole

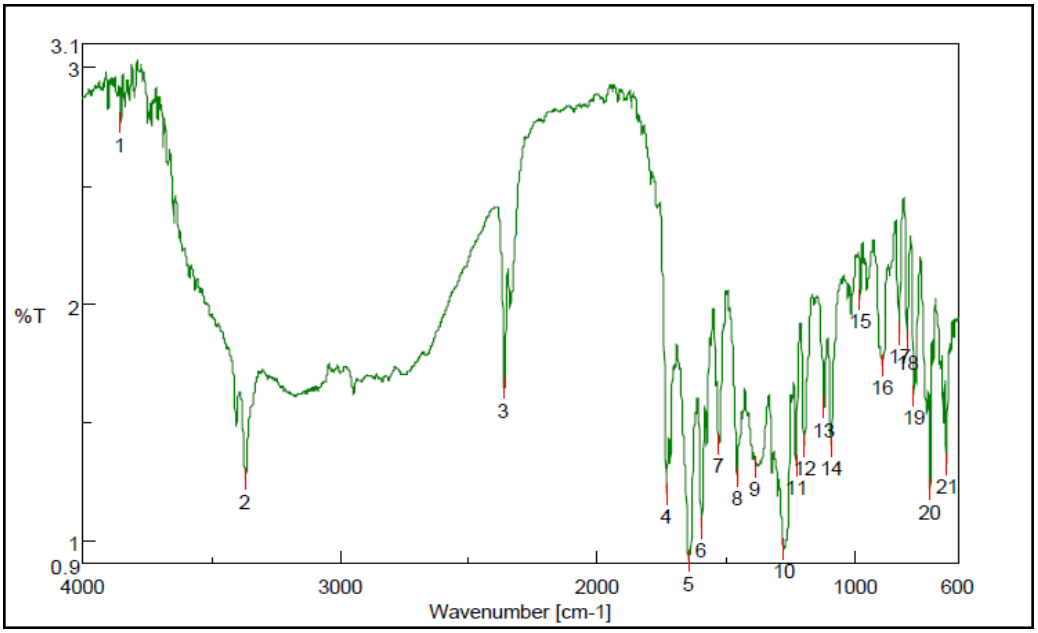

Figure: 2 FTIR Spectra of Mebendazole + Methylcellulose

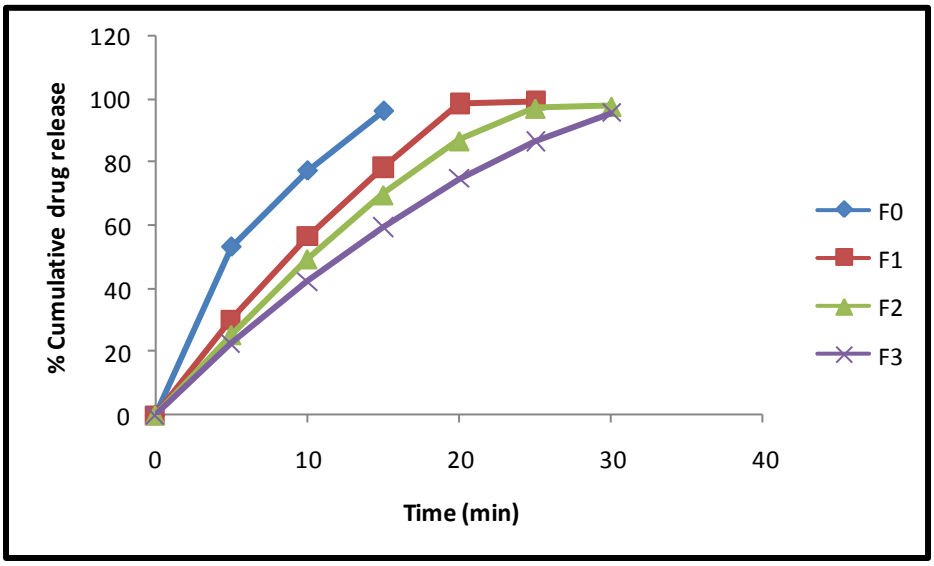

Figure :3 *In-vitro* drug release profile of formulation f0 to f3

CONCLUSION

From the above investigation it is concluded that incorporating polymer like methylcellulose can be used to formulate effective medicated lollipop. This will offer better patient compliance and innovative dosage form. Increasing the concentration of polymer like methylcellulose will lead to extended release formulation and increase the oral retention time of medicated lollipop.

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