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COMPARATIVE STUDY OF EFFECT OF DIFFERENT POLYMERS ON ALBENDAZOLE LOLLIPOPS

K. V. Nisha*[1], T. K. Ajith Babu[1], P. V. Thushara[1], K. Asna[1], N. M. Mariyam Nabeeha[1], U. K. Mohammed Shafeed[1], K. T. Shahnas[1]

[1*]Department of Pharmaceutics, Malik Deenar College of Pharmacy, Kasaragod, Kerala, India.

ABSTRACT

Helminthiasis has been reported as the major cause of under nourishment, anaemia and other related ailment associated with children of developing countries. Development of patient friendly dosage forms has always been a challenge for formulation scientists. In this study an attempt to formulate a candy based lollipop of the drug Albendazole has been tried out for treatment of helminthiasis. Heating congealing method of preparation with three hydrocolloids namely Sodium carboxy methyl cellulose, Methyl cellulose and HPMC was attempted for lollipop formulation. The formulated lollipops were evaluated for drug content, weight variation, hardness, in vitro drug release and stability. The results revealed that F1 formulation with methyl cellulose 0.5% w/w polymer showed optimum characteristics, stability and a better drug release compared to other formulations.

KEYWORDS

Albendazole, Lollipops, Helmenthiasis, MC, HPMC and Sodium CMC.

Author for Correspondence:

Nisha K V,
Department of Pharmaceutics,
Malik Deenar College of Pharmacy,
Kasaragod, Kerala, India.

Email: kvnisha0@gmail.com

INTRODUCTION

Albendazole is a potent anthelminthic benzimidazole, widely used in human helminthiasis treatment due to its efficiency against all helminth classes which usually infest animal. Since Albendazole has a very bitter taste conventional dosage forms like tablets and capsules have no paediatric acceptance.

The success of any medication depends on its patient friendly acceptance and should take to consideration during product development. Therapeutic effect will only be achieved if the patient accepts the sensory attributes of the

formulation and completes the treatment. The product appearance and flavour, regardless of its shelf life, must be fresh, agreeable and elegant since any changes in one of these aspects, may cause patient to lose confidence in the product.

MATERIAL AND METHODS

Albendazole was purchased from Yarrow Chemicals Mumbai, and other excipients were purchased from Balaji chemicals, Gujarat, Nice chemicals, Cochin, Ottokemi, Mumbai, Classic aromatics, Cochin.

Solubility study

The solubility of Albendazole was carried out in water, 0.1N HCl and Simulated salivary fluid 6.8 pH. Saturated solutions in respective solvents were prepared by adding an excess amount of drug and stirred for48 hours at 25°C using a mechanical shaker. The filtered supernatants were analysed with UV/ visible spectrophotometer at 291nm. The solubility of Albendazole in the respective liquid vehicle was calculated using calibration curve.

Determination of drug- polymer compatibility

FTIR can be used to investigate any physiochemical interaction between different excipients. FTIR spectral matching approach was used for detection of any possible chemical interaction between drug and polymer. FTIR spectral analysis of pure drug and selected polymers were carried out individually and as physical mixtures. The samples of Albendazole, Methyl Cellulose, Hydroxy Propyl Methyl Cellulose and Sodium Carboxy methyl cellulose were prepared and stored at temperature of 40 ± 2°C/75 ± 5% RH for 1 month. After 1 month they were subjected to FTIR spectral analysis. The samples were placed in FT-IR window after mixing and triturating with potassium bromide.

Method of preparation of medicated lollipop

Medicated lollipops of Albendazole were prepared using heating and congealing technique. They were prepared. The required quantity of sucrose was dissolve into water. Dextrose was dissolved in small quantity of water and heated it to 110°C till dextrose dissolves completely forming as clear viscous syrup .Then the dextrose syrup was poured into the sucrose syrup and heated to 160°C till the colour changes to golden yellow. Raspberry flavour was added between 120°C to 135°C. Then temperature was bought down to 90°C and Albendazole, polymer, glycerol, PEG, glycerol, methyl paraben, citric acid were added and mixed it well. The prepared mixture was poured into the calibrated mold and kept it for air drying for 1-2 hr. The prepared lollipops were wrapped in aluminium foil and stored in desiccators to prevent moisture uptake.

Three polymers (methyl cellulose, Na CMC and HPMC) were used in preparation of lollipop. In the first trial methyl cellulose was employed as polymer and four different batches F1, F2 and F3 are prepared with concentration 0.5, 1.0, 1.5 and of total weight of one lollipop. Similarly formulations F4, F5, F6, with Na CMC and F7, F8, F9, was prepared with HPMC. A batch without lollipop forming polymer F0 was formulated.

EVALUATION OF MEDICATED LOLLIPOPS

Evaluation of Physical appearance

Physical appearance of prepared medicated lollipop of Albendazole was evaluated.

Weight variation

The weight variation tests were done as per the procedure mentioned in USP 2007.10.

Lollipops were weighed and their average weight was determined. Individual weight of Lollipops was compared with the average weight and variation was determined.

$$\text{Weight Variation} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Final weight}} \times 100$$

Hardness

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

Thickness

Thickness was measured using vernier callipers. It was determined by checking the diameter of 10 lollipops of each formulation.

Friability

The friability of the lollipops was determined by using Roche Friabilator. 10 lollipops were weighed

and placed in the friabilator and operate for 4min at 25 rpm. The lollipops are then dedusted and reweighed. The percentage friability is calculated by using the formula.

% Friability = $\frac{W_0 - W_1}{W_0} \times 100$

W_0:-Initial weight of 10 lollipops

W_1:-Final weight of 10 lollipops

Drug content

Drug content test were done for 10 lozenges, where each lozenges were taken and powdered and dissolved in to simulated salivary fluid and volume made up to 100ml with simulated salivary fluid. Absorption was measured at 291nm and drug content calculated using calibration curve.

***In-vitro* release studies**

Dissolution in Official Media

All formulations were subjected to in-vitro release study in 0.1N HCl pH-1.2 which is the official media. It was carried out in USP type 2 dissolution apparatus, at temperature of 37±0.5ºC and stirred at 50rpm. The samples were withdrawn at predetermined time intervals with same volume of fresh medium being replaced after each withdrawal. The sample was suitability diluted and absorbance was measured at 291nm.

Dissolution in Simulated Salivary Fluid

In-vitro dissolution profile from Albendazole lollipops was carried out in a beaker containing 10ml of Simulated Salivary Fluid (p^H-6.8) and maintained at 37 $\pm$ 0.5ºC. The medium was stirred at 50rpm using magnetic stirrer. Aliquots (5ml) of dissolution medium were withdrawn at 5, 10, 15, 20, 30, 45, 60 time intervals and the sample was replaced with fresh medium. Samples were analyzed by UV spectrophotometer at 291nm.

Stability studies

Stability is defined as the extent to which a product retains its characteristic within specified limits throughout its period of storage and use (i.e., its shelf life). Stability testing is performed to ensure that the drug products retain their fitness for use until the end of their expiration dates. Optimised lollipop formulation was subjected to stability studies at 40ºC and 75% RH for a period of 45 days and was evaluated for drug content and in vitro drug release.

RESULTS AND DISCUSSIONS

Solubility study

From the study, the solubility profile of Albendazole was slightly soluble in water, soluble in 0.1N HCl and simulated saliva.

Determination of melting point

The melting point was determined by capillary tube method. The melting temperature of pure sample of Albendazole recorded at 178ºC which complies with the official standard indicating the purity of the sample.

Drug-polymer compatibility by FT-IR studies

After spectral comparison it was confirmed that all characteristic peaks of Albendazole observed in its pure drug was observed in the physical mixture of formulation and the final optimized formulation. There was no new peak or disappearance of characteristic peak. The FT - IR spectrum of standard drug Albendazole and its physical mixture with polymers correspond to the similar wave numbers. This indicates that there is no interaction between drug and polymers and that polymers and the drug are compatible with each other.

EVALUATION OF MEDICATED LOLLIPOP

Physical appearance of prepared lollipops

From the evaluation of physical appearance, it was evident that without hydrocolloid polymer the characteristic consistency of lollipop could not be achieved. 0.5% - 1.5% w/w concentrations of MC, NaCMC and HPMC resulted in ideal lollipops with respect to appearance and elegance. 2% w/w Concentration of hydrocolloid lollipops was found to be sticky. Hence it was concluded that 0.5% w/w - 1.5% w/w of hydrocolloids can be fixed as optimum concentration. (F1 to F9) batches were subjected for further evaluation.

Study of weight variation

From the results of weight variation test, it was observed that all formulations pass the limits for the test. Weight varied from range of ± 0.99% to ± 3.6%.

Study of hardness

Hardness for all lollipops was found out and it was observed in range of 8.83 ± 0.15 to 10.26 ± 0.15 kg/cm². The results were found to be satisfactory.

Study of Thickness

The thickness for all formulations was found to be between 5.90 ± 0.15 to 5.93 ± 0.15mm and it was found to be satisfactory.

Study of Friability

The friability was in the range of 0.31 ± 0.015-0.35 ± 0.005 and was found satisfactory.

Study of drug content

The drug content for all formulations was found to be varying between 98.7 ± 0.43 to 99.8 ± 0.36. The high drug content indicates that the selected method is suitable for manufacturing of lollipops.

***In vitro* drug release**

In vitro dissolution studies of formulated lollipops were done in 0.1HCl as per the method described in methodology. Lollipops with polymer Methyl cellulose 0.5, 1, 1.5% (F1-F3 batch), sodium carboxy methylcellulose (F4-F6 batch), HPMC polymer (F7-F9 batch) were evaluated for *in vitro* drug release study.

It was observed that in F1 batch, almost complete release of 98.9% occurred in 20minutes compared to 98.8% in 25 minutes in F2 and 8.3 % in 30min in F3. It was clear that as concentration of methyl cellulose increased there was slight delay in drug release. The dissolution studies revealed that 98.4% drug release in 30 minute in F4 compared to 93.2% and 89.7% in F5 and F6 respectively. It was fond that increase in concentration NaCMC, here was a sustained release of drug. A similar drug release behaviour as lollipops formulated with MC and NaCMC was observed here. There was a comparatively faster release of 96.63% in 30minute in F7 followed by delay in release with 90.2% and 84.3% release in F8 and F9. The evaluation of the optimised formulation after stability charging showed there was no significant change observed in the results of *in- vitro* dissolution study. Thus the above study showed that Albendazole lollipop was stable during the study.

Table No.1: Formulation of Albendazole lollipops

S.No	Ingredients (g)	F0	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Albendazole	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
2	Sucrose	1.30	1.30	1.30	1.30	1.30	1.30	1.30	1.30	1.30	1.30
3	Dextrose	0.366	0.366	0.366	0.366	0.366	0.366	0.366	0.366	0.366	0.366
4	Methyl cellulose	-	0.5	1.0	1.5	-	-	-	-	-	-
5	Sodium CMC	-	-	-	-	0.5	1.0	1.5	-	-	-
6	HPMC	-	-	-	-	-	-	-	0.5	1.0	1.5
7	Glycerol	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.02	0.02	0.02
8	PEG	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	O.O2	0.02
9	Methylparaben	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002
10	Citric acid	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
11	Amaranth	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002	0.002
12	Raspberry	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
13	Water	q.s.	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
14	Total weight	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00	2.00

Table No.2: Physical parameters of Albendazole lollipop

S.No	Formulation	Weight variation (± %)	Hardness (Kg/cm^2)	Thickness (mm)	Friability %	Drug content (%±SD)
1	F1	2.4	9.26±0.20	5.91±023	0.35±0.004	99.8±0.36
2	F2	1.45	9.56±0.30	5.92±0.21	0.35±0.005	99.2±0.42
3	F3	3.6	10.26±0.15	5.90±0.15	0.31±0.015	98.9±0.22
4	F4	0.99	10.25±0.12	5.92±0.14	0.32±0.104	99.2±0.45
5	F5	2.34	9.56±0.20	5.91±0.13	0.32±0.005	98.9±0.34
6	F6	2.67	9.63±0.15	5.91±0.15	0.32±0.014	98.2±0.55
7	F7	2.55	9.63±0.15	5.92±0.15	0.31±0.005	99.2±0.55
8	F8	3.45	8.83±0.15	5.93±0.15	0.32±0.006	99.1±0.53
9	F9	3.20	10.22±0.15	5.93±0.15	0.32±0.005	98.7±0.43

Table No.3: *In-vitro* drug release from F1-F5

S.No	Time (min)	% Cumulative drug release of Formulations				
		F1	F2	F3	F4	F5
1	0	0	0	0	0	0
2	5	24.3±0.01	22.6±0.02	19.3±0.012	21.5± 0.015	18.3 ±0.003
3	10	48.2±0.015	44.4±0.02	40.4±0.002	46.2± 0.02	38.2± 0.02
4	15	70.1±0.005	68.3±0.03	59.8±0.01	60.8± 0.013	58.0 ±0.01
5	20	98.9±0.01	89.2±0.015	78.1±0.012	73.3 ±0.005	69.2± 0.012
6	25	97.8±0.02	98.8±0.012	92.5±0.01	80.2± 0.012	78.6 ±0.015
7	30	96.7±0.02	97.2±0.002	98.3±0.01	98.4± 0.02	93.2 ±0.01

Table No.4: *In-vitro* drug release from F6-F9

S.No	Time (min)	% Cumulative drug release of Formulations			
		F6	F7	F8	F9
1	0	0	0	0	0
2	5	16.2 ±0.01	18.2± 0.01	14.3± 0.02	10.8 ±0.02
3	10	24.4 ±0.02	32.8± 0.02	24.6± 0.02	20.3 ±0.015
4	15	32.2 ±0.01	56.4± 0.012	42.8 ±0.01	39.4± 0.005
5	20	52.8 ±0.01	70.2 ±0.01	63.2 ±0.02	58.4± 0.02
6	25	69.2± 0.02	83.3± 0.015	76.4± 0.02	70.2± 0.02
7	30	89.7 ±0.02	96.3± 0.02	90.2 ±0.005	84.3 ±0.015

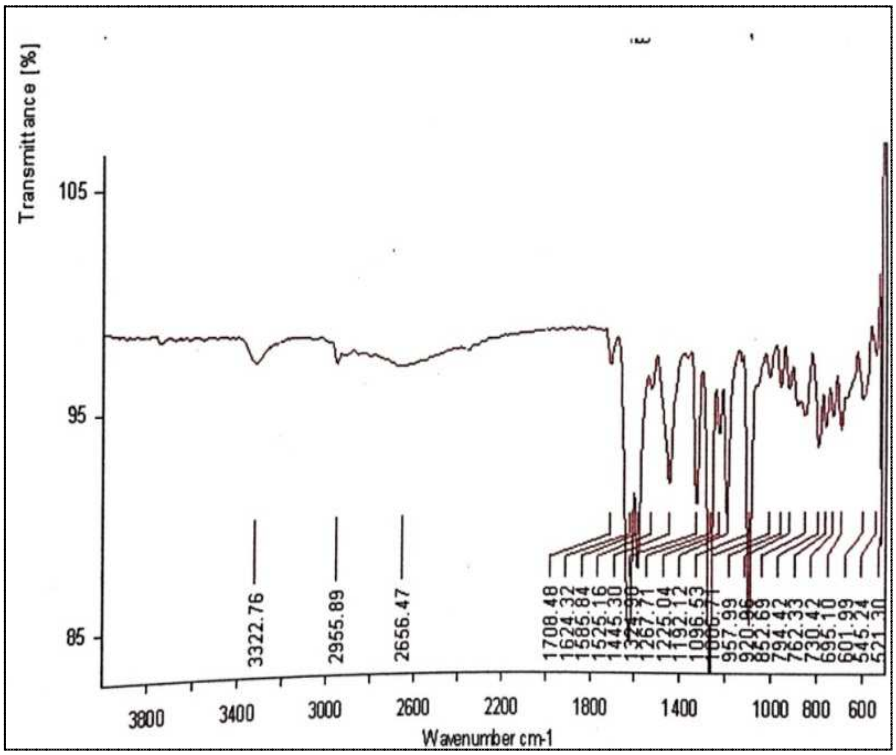
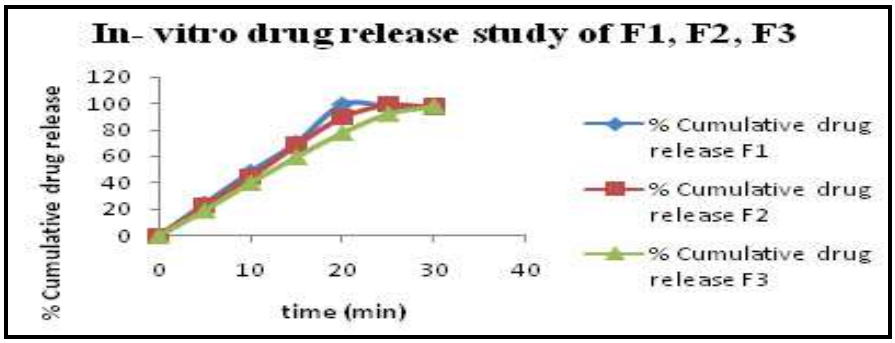
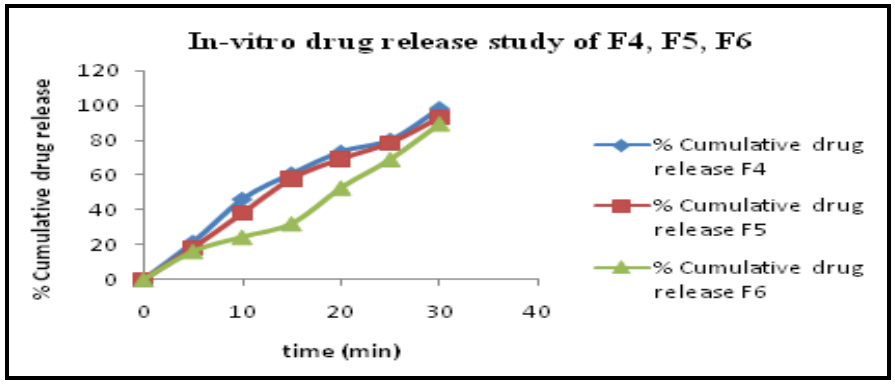


Figure No.1: FT - IR Characterization of (with MC)





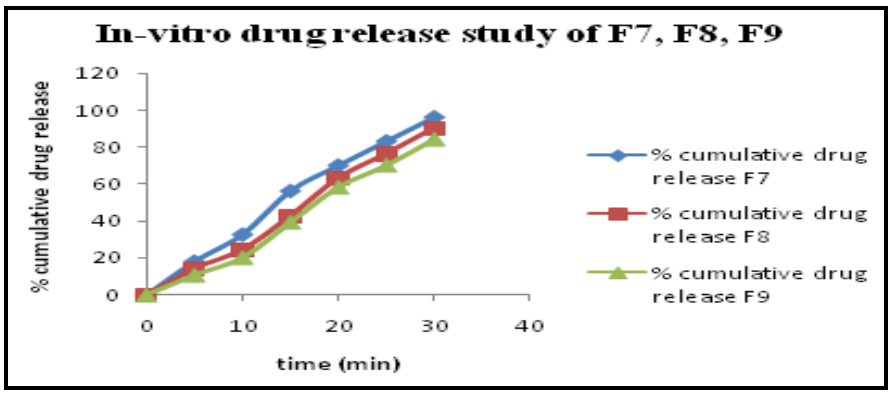


Figure No.2: *In-vitro* drug release studies result formulations F1-F9

CONCLUSION

This study concluded that medicated lollipop has been reflected as one of the contemporary advancement in the paediatric dosage form. But further clinical study and scale up study should be done to substantiate the potential of this novel dosage form.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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