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FORMULATION AND EVALUATION OF CANDY DOSAGE FORM OF ALBENDAZOLE FOR PAEDIATRICS

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Abstract : Candy are flavored medicated dosage form intended to be sucking and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base. Medicated candy is designed to improve patient compliance, acceptability. Albendazole is a broad-spectrum anthelmintic. It is widely used for the management and treatment of intestinal nematode infection. This project concluded the possibility of developing Albendazole Candy by heating and congealing method using methylcellulose, citric acid as polymer. The dissolution was carried out in USP II paddle type dissolution apparatus.
The Physiochemical properties like general appearance of albendazole, preformulation evaluation i.e tapped density, bulk density, Hausner's ratio, angle of repose and solubility and post formulation evaluation i.e weight variation, drug content uniformity and drug dissolution were evaluated of different batches or formulation from F1 to F9 which complies the specifications. The drug release was best fitted to model depended zero order release kinetics and Formulation 5 is the better formulation among all. Also using similarity and dissimilarity factor, from the obtained results it is clear that the drug release from the nine formulations are highly similar.

CHAPTER I
INTRODUCTION

1.1 Background

1.1.1 Oral Route Of Drug Delivery

The oral route is one of the most preferred routes of drug administration as it is more convenient, cost effective, and ease of administration lead to high level of patient compliance. The oral route is problematic because of the swallowing difficulty for pediatric and geriatric patients who have fear of choking. Patient convenience and compliance oriented research has resulted in bringing out safer and newer drug delivery systems[Bala R, Pawar P, Khanna S, and Arora S, 2013].
The administration of the drug according to the dose regimen and the dose regimen is specially made according to the patient life style. By oral route drug administration, the drug passes through the GIT, the drug is released from the dosage form in a solution at or near the optimal site for drug absorption to occur.GI fluid volume and motion can vary remarkably which has importance on drug dissolution and absorption.[Gade, Sonali T., 2020]
Solid dosage form means capsules or tablets or similar legend drug products intended for administration and which could be ingested orally.

Candy

Candy are flavored medicated dosage form intended to be sucking and held in the mouth or pharynx containing one or more medicaments usually in the sweetened base. Medicated candy is designed to improve patient compliance and acceptability[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019].

The benefits of the medicated candy is they increase the retention time of the dosage form in oral cavity which increases bioavailability, reduces gastric irritation and bypasses first pass metabolism. Difficulty in swallowing (dysphagia) is a common problem of all age groups, especially the elderly and paediatrics, because of physiological changes associated with those groups[Rathod M, Poharkar S, Pandhre Y, Muneshwar M, Sul S, 2018].

A drug can be administered via a many different routes to produce a systemic pharmacological effect. The oral route of drug administration is the most important method of administering drug for systemic effect[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019].

Type of candy

Hard candy: Hard candy might be considered solid syrups of sugars. These dosage forms are made by heating sugars and other ingredients together and then pouring the mixture into a mould[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019].

Soft candy: They are either meant for chewing or for slow drug release in mouth. They can be hand rolled and then cut into pieces or the warm mass can be poured into a plastic mould[Rathod M, Poharkar S, Pandhre Y, Muneshwar M, Sul S, 2018].

1.1.2 Drug specific review

Albendazole is chemically described as **methyl *N*-(6-propylsulfanyl-1*H*-benzimidazol-2-yl)carbamate .** Albendazole inhibit the effect on tubulin polymerization which results in the loss of cytoplasmic microtubules, inhibition of micotubule-dependent glucose-up-take significantly. Albendazole is practically insoluble in water but slightly soluble in solvents like chloroform, methanol, ethyl acetate, and acetonitrile. The detail description of drug is given in Table and Figure below:

Table 1.1: physicochemical properties of albendazole

IUPAC	methyl *N*-(6-propylsulfanyl-1*H*-benzimidazol-2-yl)carbamate
Bioavailability	Less than 5%
Metabolism	Liver
Biological half-life	8.5 hours (8-12 hrs for single dose of 400mg)
Excretion	Renal excretion(kidney)
Formula	C12H15N3O2S
Molecular mass	265.33g/mol
Plasma protein binding	**70%**

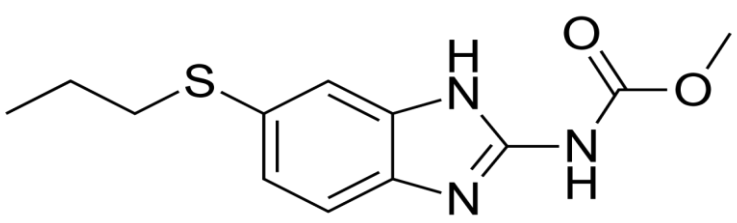

figure 1.1 chemical structure of albendazole

Albendazole(benzimidazole carbamate) is a broad-spectrum anthelmintic(agents that kill parasitic worms)[Kar Ashutosh, 2007].

It is widely used for the management and treatment of intestinal nematode infection. It is also quite effective as a single-dose-treatment for ascariasis, hookworm infections, and trichuriasis[Kar Ashutosh, 2007].

It has been observed that a recommended multi-dose therapy with albendazole may help in the complete eradication of pinworm, threadworm, capillariasis, chlonorchiasis, and hydated disease as well[Kar Ashutosh, 2007].

Side effects[Tripathi KD,2013]

- Albendazole is well tolerated; only gastrointestinal side effects have been noted.
- Few patients have felt dizzines.
- Prolonged use, as in hydatid or in cysticercosis, has caused headache, fever, alopecia, jaundice and neutropenia.

1.1.3 Advantages of Buccal Drug Delivery system[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019]

- Bypass of the gastrointestinal tract and hepatic partake system, increasing the bioavailability of orally administered drug that otherwise undergo hepatic first-pass metabolism. In addition, the drug is protected from degradation due to pH and digestive enzyme of the middle gastrointestinal tract.
- The large contact surface of the oral cavity contributes to rapid and extensive drug absorption.
- Oral mucosal delivery occurs is less variable between patients, resulting in lower inter-subject variability as compared to transdermal patches.
- Improved patient compliance due to the elimination of associated pain with injections; convenience of administration as compared to injections or oral medication.
- Sustained drug delivery.
- A relatively rapid onset of action can be achieved relative to the oral route, and the formulation can be removed if therapy is required to be discontinued.
- Increased ease of drug administration.
- In comparison to TDDS, mucosal surface does not have a stratum corneum. Thus, the major barrier layer to transdermal drug delivery is not a factor in oral mucosal routes of administration. Hence oral mucosal systems exhibit a faster initiation and decline of delivery than do transdermal patches.
- Though less permeable than the sublingual area, the buccal mucosa is well vascularized, and drugs can be rapidly absorption into the venous system underneath the oral mucosa.

1.1.4 Limitation of Buccal Drug Delivery System[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019]

- For local action the rapid elimination of drug due to the flushing action of saliva or the ingestion of foods stuffs may lead to the requirement for frequent dosing.
- The non-uniform distribution of drug within saliva on release from a solid or semisolid delivery syatem could mean that some areas of the oral cavity may not receive effective levels.
- For both local and systemic action, patient acceptability in terms of taste, irritancy and 'mouth feel' is an issue.
- For systemic delivery the relative impermeability of oral cavity mucosa with regard to drug absorption, especially for large hydrophilic biopharmaceuticals, is a major concern.

1.1.5 ADME

Poorly absorbed from the gastrointestinal tract due to its low aqueous solubility.

Oral bioavailability of albendazole appears to be increased when the drug is administered with a fatty meal; when the drug is administered with meals containing about 40 g of fat, plasma concentrations of albendazole sulfoxide(which has potent anthelmintic activity) are up to 5 times higher than those observed when the drug is administered to fasting patients[McEvoy, G.K.,2005].

Albendazole sulfoxide is about 70% bound to plasma proteins and has a highly variable plasma half-life ranging from about 4 to 15 hr. It is well distributed into various tissues, including hydatid cysts, where it

reaches a concn of about one-fifth that in plasma. This probably explains why albendazole is more effective than mebendazole for treating hydatid cyst disease[O'Neil, M.J.,2001].

Albendazole is rapidly metabolized in the liver and possibly in the intestine as well, to albendazole sulfoxide(which is further metabolized to albendazole sulfone and other primary oxidative metabolites that have been identified in human urine.), which has potent anthelmintic activity[Hardman, J.E., L.E. Limbird,P.B., A.G. Gilman ,Goodman and Gilmans].

Urinary excretion of albendazole sulfoxide is a minor elimination pathway with less than 1% of the dose recovered in the urine. Biliary elimination presumably accounts for a portion of the elimination as evidenced by biliary concentrations of albendazole sulfoxide similar to those achieved in plasma[[Hardman, J.E., L.E. Limbird,P.B., A.G. Gilman ,Goodman and Gilmans].

1.1.6 Composition Of Oral Mucosal Layer

The oral mucosal layer consists of 95% of water, Glycoprotein and lipids 0.5-5% and mineral salts 1% & free protein between 0.5-1%. [https://en.wikipedia.org/wiki/Oral_mucosa]

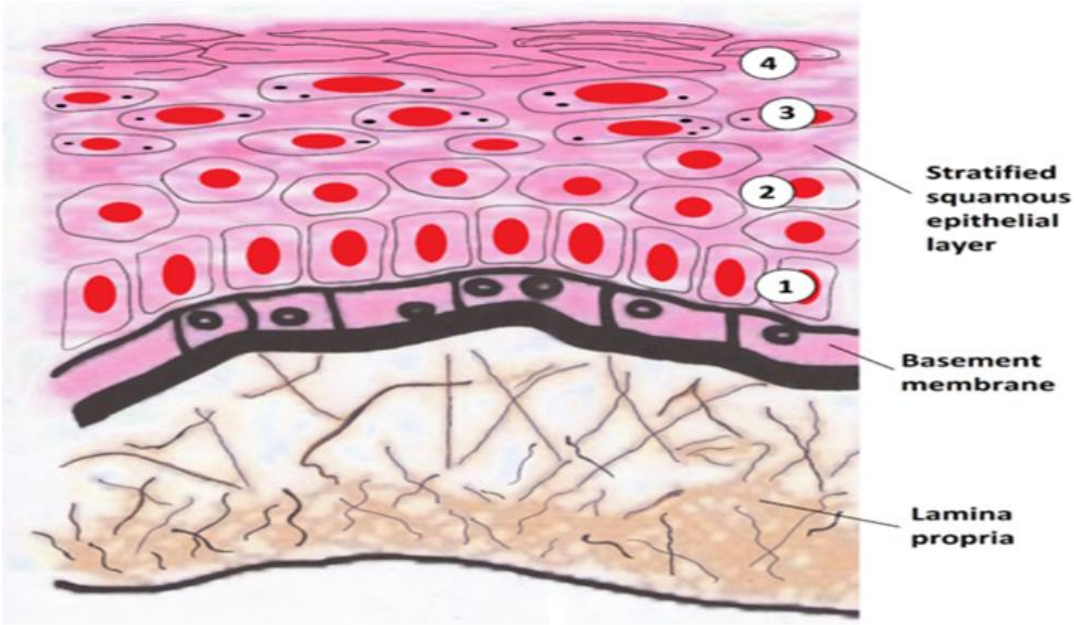

figure 1.2: structure of oral mucosa layer

1.1.7 Mechanism of Action

The principal mode of action for albendazole is by its inhibitory effect on tubulin polymerization which results in the loss of cytoplasmic microtubules, inhibition of micotubule-dependent glucose-up-take significantly[Kar Ashutosh, 2007].

The mode of action of albendazole is by binding strongly with the tubulin in the cells of nematodes. The intestinal cells of the nematode are particularly affected, resulting in a loss of absorptive function which causes the nematodes to starve to death[O'Neil, M.J.,2001].

1.2 Statement of problem

The dosage forms of albendazole are also available as oral solution, syrups, tablet and injection etc. but there are several reasons to select this drug for a candy dosage form.

Albendazole absolute oral bioavailability is less than 5% in humans. After oral administration, it rapidly undergoes first-pass metabolism in the liver. Also non compliance occurs sometime in case of chewable tablets of albendazole.

Therefore formulating albendazole in candy dosage form can eliminate the first pass metabolism and enhance the bioavailability also if taken with fatty meal further bioavailability will be increased. Also we can increase the patient compliance.

1.3 Rationale of study

The rationale behind this study is to formulate and evaluate the albendazole in candy dosage form for paediatrics .

Since the drug absolute oral bioavailability is **less than 5%** in humans. After oral administration, it rapidly undergoes first-pass metabolism in the liver, an attempt is made to develop candy dosage form of

albendazole. This could be applied to paediatric and some dysphagic patients and avoid first pass effect for improvement in bioavailability. Also, to improve patient compliance.

CHAPTER III

3. MATERIAL AND METHODOLOGY

3.1 Raw materials:

Albendazole and other excipients like Sucrose, Dextrose, Methylcellulose, Glycerine, Quinoline Yellow, Pineapple flavor and Citric acid were provided by Time Pharmaceuticals Pvt. Ltd. Other materials required were provided by Shree Medical and Technical College as shown in **Table 3.1.**

Table 3.1: raw materials

Active pharmaceutical materials	Albendazole
Sugar /saccharides	Sucrose,Dextrose
Binder	Methylcellulose
Lubricant	Glycerine
Colouring agent	Quinoline Yellow
Flavouring agent	Pineappleflavor
Preservative & Polymer	Citric acid

3.2 Reagents required:

All the reagents were provided by Shree Medical and Technical College as follows:

- Dimethyl formamide
- 0.1N HCl

3. 3 Instruments and devices

The list of instruments and devices which were used during this project are listed in **Table 3.2.**

Table 3.2: instruments and devices requirement for formulation:

Analytical precision balance	Mould
Mixing vessels	UV-visible spectrophotometer
Heating vessels/chamber	Heating mantle
Thermometer	Dissolution test apparatus
Desiccators	Electromagnetic stirrer
Aluminium foil /plastics	Glass Rod

3.4 Study Design

It was an experimental study because the new candy of albendazole has been formulated.

3.5 Study method

Both qualitative and quantitative study method were used. Qualitative methods include appearance of candy. Quantitative study includes all evaluation procedure such as weight variation, assay/content uniformity and in-vitro dissolution study.

3. 6 Study area

This project work were carried out in the laboratory of Shree Medical & Technical College, Bharatpur-12, Chitwan Nepal.

3. 7 Study period

This project work was completed in 6 months after proposal defense.

3. 8 Preparation of Calibration Curve

3. 8.1 Preparation of Calibration Curve using 0.1N HCl

Ten mg of albendazole was dissolved in few amount of methanol and was diluted to 100 ml using 0.1N HCl to prepare primary stock solution. From this solution suitable volume was withdrawn and diluted with 0.1N HCl to get 2,4,6,8 and10 mcg/ml solution and absorbance was taken at 291nm. Then the graph was plotted taking concentration in x-axis and absorbance in y-axis. Regression equation and correlation coefficient was obtained from graph.

3.8.2 Preparation of Calibration Curve using dimethyl formamide and 0.1N HCl for Assay

Ten mg of albendazole was taken and dispersed in dimethyl formamide and diluted to 100 ml using 0.1N HCl to prepare primary stock solution. From this solution suitable volume was withdrawn and diluted with 0.1N HCl to get 2,4,6,8 and 10 mcg/ml solution and absorbance was taken at 291nm.. Then the graph was plotted taking concentration in x-axis and absorbance in y-axis. Regression equation and correlation coefficient was obtained from graph.

3.9 Formulation

Nine different batches of albendazole candies having label strength of 200 mg were prepared by heating and congealing method. The products were coated as F1 to F9. The details of formulations of albendazole candies was shown in **Table 3.3.**

Table 3.3: formulation table:

Ingredient	F1 (gm)	F2 (gm)	F3 (gm)	F4 (gm)	F5 (gm)	F6 (gm)	F7 (gm)	F8 (gm)	F9 (gm)
Albendazole	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Sucrose	3	3	3	3	3	3	3	3	3
Dextrose	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Methyl Cellulose	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16
Citric acid	0.192	0.192	0.192	0.192	0.192	0.192	0.192	0.192	0.192
Glycerin	0.5%	1%	1.5%	2%	2.5%	3%	3.5%	4%	4.5%
Quinoline Yellow color	qs	qs	qs	qs	qs	qs	qs	qs	qs
Pineapple flavor	qs	qs	qs	qs	qs	qs	qs	qs	qs

3.10 Method Of Preparation

The candy was prepared by heating and congealing method using methylcellulose, citric acid as polymer. Pourability, Texture and Elasticity was due to different plasticizers like glycerin.

Required quantity of sugar syrup was prepared by mixing sugar with water. Dextrose was dissolved in small quantity of water and it was heated to110°C till dextrose dissolves completely forming as clear viscous syrup. Then the dextrose syrup was poured into the sugar syrup and was heated to 160°C till the colour changes to golden yellow. Flavour was added between 120°C to 135°C then temperature was bought down to 90°C and drug, polymer and other ingredients were added and mixed it well. The prepared mixture was poured into the calibrated mould and it was kept for air dry for1-2 hrs. The prepared candies were stored wrapped in aluminum foil and stored in desiccators to prevent moisture uptake[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019]. Flowchart showing preparation of candy was shown in **Figure No. 3.1**

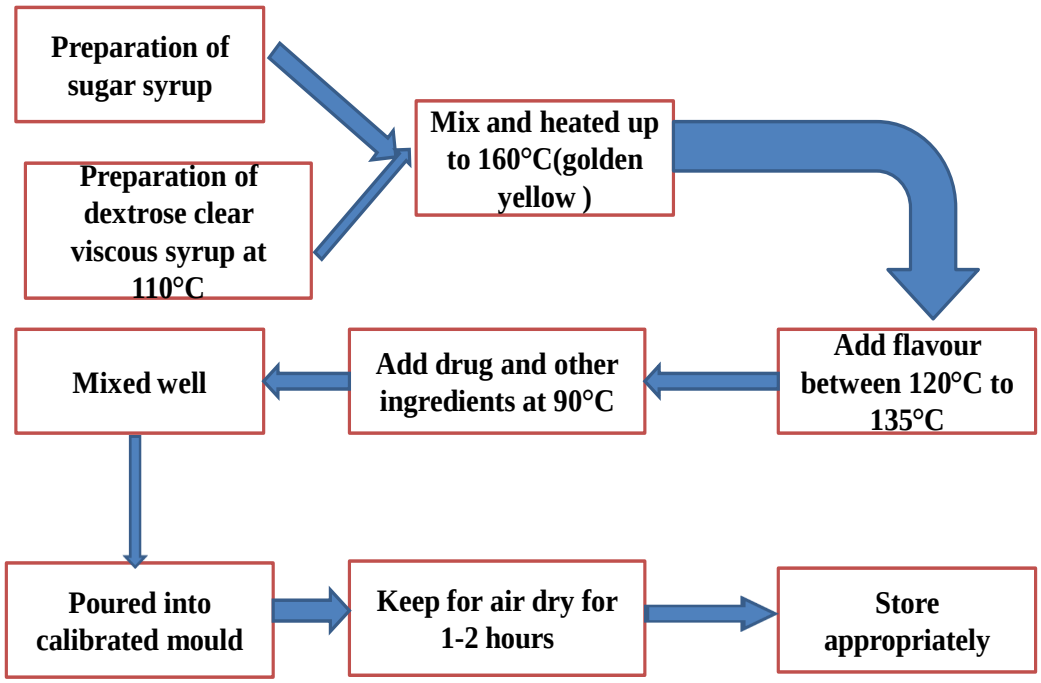

Figure No. 3.1: flowchart showing preparation of candy

3.11 Pre-Formulation Evaluation

3.11.1 Physical Properties

The following physical properties like state of matter, color, odour, texture, melting point were evaluated[O'Neil, M.J.,2001].

3.11.2 Tapped density

The measuring cylinder containing known mass of blend was tapped for a fixed time. The minimum volume (Vt) occupied in the cylinder and weight of powder blend (W) were measured[Palanichamy S, Anusha V, Solairaj P, Parasakthi N, Rajadhas G, Thanga Thirupathi A., 2011]. The tapped density (TBD) was calculated using the formula;

TBD= Weight of the powder(W)/Tapped volume(Vt)……..eq 3.1

3.11.3 Bulk density

Bulk density or Apparent density (LBD) was determined by pouring blend into a graduated cylinder. The bulk volume (Vo) and weight of powder (W) were determined[Palanichamy S, Anusha V, Solairaj P, Parasakthi N, Rajadhas G, Thanga Thirupathi A., 2011]. The bulk density(BD)was calculated using the formula;

LBD= Weight of powder(W)/Bulk Volume(V_0)……eq 3.2

3.11.4 Hausner's ratio

It is the ratio of tapped density to the bulk density. It provides an indication of the degree of densification which could result from vibration of the feed hopper.it was calculated by;

Hausner's ratio = Tapped density/ Bulk density……eq 3.3

Lower Hausner's ratio indicates better flow ability while higher hausner's ratio indicates poor flow ability as shown in **Table 3.4.**

Table 3.4: relationship between hausner's ratio and flow character.

Flow character	Hausner's ratio
Excellent	1.00-1.11
Good	1.12-1.18
Fair	1.19-1.25
Passable	1.26-1.34
Poor	1.35-1.45
Very poor	1.46-1.59
V. very poor	>1.60

3.11.5 Flow property (Angle of repose)

Angle of repose was determined using fixed funnel method. The blend was poured through a funnel that was raised vertically until a maximum cone height (h) was obtained[Palanichamy S, Anusha V, Solairaj P, Parasakthi N, Rajadhas G, Thanga Thirupathi A., 2011]. Radius of the heap (r) was measured and angle of repose was calculated using formula as given in equation no.3.4.

$$\theta = \tan^{-1}(2h/d)$$

$$\theta = \tan^{-1}(h/r) \quad \text{.....eq 3.4}$$

Where, θ is angle of repose, h is height of pile and r is the radius of the base pile.

Table 3.5: Relationship between angle of repose and flow properties

Angle of Repose (θ) (degree)	Flow properties
< 25	Excellent
25-30	Good
30-40	Passable
>40	very poor

3.11.6 Solubility

Small amount of Albendazole was taken and different solvent like chloroform, methanol, ethyl acetate, and acetonitrile were added separately and solubility was determined.[Azad AK, Jahan K, Sathi T, Sultana4 R, Abbas S, UddinUddin A., 2018].

3.12 Post Formulation Evaluation

3.12.1 Weight variation

Twenty candies were taken and weighed individually. Average weight was calculated and compared the individual candy weight to the average weight. The requirements was met if the weights of not more than two of the candy differ from the average weight by more than the percentage listed in the accompanying table and no candy differs in weight by more than double that percentage[Punam V. Chaudhari*, Nirma G.Chaudhari, Pooja S .Chaudhari, Amruta M.Patil., Sunil P.Pawar.,2019]

3.12.2 Drug content uniformity

The drug content was estimated for all the formulations of medicated candy. Candy from each batch was selected and weighed individually and dispersed in dimethyl formamide.Then it was placed in magnetic stirrer after addition of 0.1 N HCl for 30 min. The final volume was made to 100ml using 0.1N HCl. The solution was diluted suitably, and analyzed spectrophotometrically at 291 nm using UV-visible double-beam spectrophotometer[Chaudhari P V, Chaudhari NG, Chaudhari PS, Patil AM, Pawar SP, 2019].

3.12.3 Dissolution test

Dissolution study was conducted for all the formulation using USP type-II apparatus. The dissolution test was performed using 900ml of 0.1N HCl as the dissolution medium at 50 rpm and 37°C±0.5°C. Sample 10 ml was withdrawn at 15, 30, 45 and 60 minutes interval and diluted suitably with 0.1N HCl and the sample volume was replaced with an equal volume of fresh dissolution medium. The sample was analyzed spectrophotometrically at 291nm after suitable dilution. [Palanichamy S, Anusha V, Solairaj P, Parasakthi N, Rajadhas G, Thanga Thirupathi A., 2011]

3.12.4 Data Analysis

Data analysis was done by using ddsolver Microsoft excel 10, obtained dissolution data was fitted in different model dependent (zero, first order kinetics) and model independent method (similarity and dissimilarity factor).

CHAPTER IV

4. RESULTS AND DISCUSSION

4.1 Calibration Curve

4.1.1 Preparation of Calibration Curve using 0.1N HCl

Reference standard 10mg Albendazole was dissolved in small volume of methanol and was diluted to 100 ml using 0.1N HCl to prepare primary stock solution. Then it was diluted to 2,4,6,8 and10 mcg/ml using 0.1N HCl and absorbance were observed. Then the graph was plotted taking concentration in x-axis and absorbance in y-axis. The graph is shown in **Figure 4.1.** The correlation coefficient($R^{2)}$ obtained from the graph is 0.998. The regression equation obtained from graph is shown in equation no. 4.1. The equation obtained from the calibration curve is used to calculate drug release.

y=0.110x+0.031…….eqn no.4.1

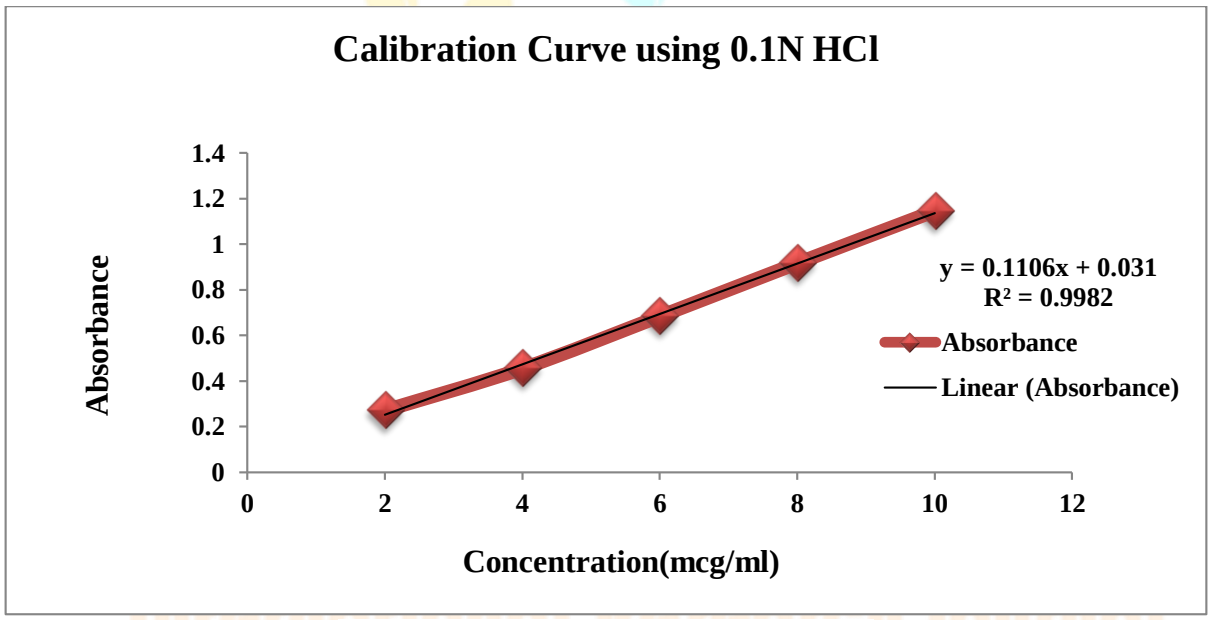

Figure 4.1: Calibration Curve using 0.1 N HCl

4.1.2 Calibration Curve using dimethyl formamide and 0.1N HCl for Assay

Reference standard 10mg Albendazole was dispersed in few volume of dimethyl formamide and was diluted to 100 ml using 0.1N HCl to prepare primary stock solution. Then it was diluted to 2,4,6,8 and 10 mcg/ml using 0.1N HCl and absorbance were observed. Then the graph was plotted taking concentration in x-axis and absorbance in y-axis. The graph is shown in **Figure 4.2.** The correlation coefficient($R^{2)}$ obtained from the graph is 0.999. The regression equation obtained from graph is shown in equation no. 4.2. The equation obtained from the calibration curve is used to calculate the drug content from the formulation.

y=0.067x+0.012……. eqn.no. 4.2.

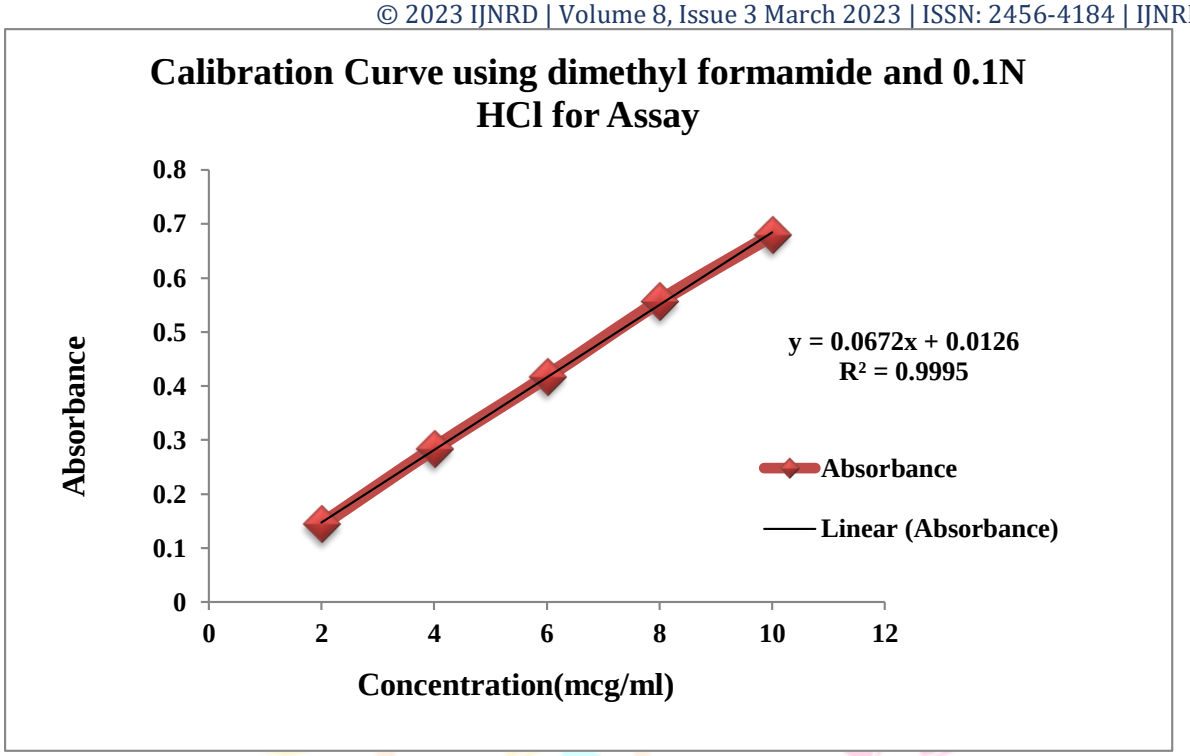

Figure 4.2: Calibration Curve using dimethyl formamide and 0.1N HCl for Assay

4.2 Evaluation of Active Albendazole

Physical Properties of Albendazole were examined and the results are shown in **Table 4.1.**

Table 4.1: physical properties of albendazole

Physical Properties	Results
State of Matter	Fine Powder (Solid)
Color	White
Odour	Odourless
Texture	Smooth
Melting Point	208°C

4.3 Pre Compression Evaluation

4.3.1 Tapped density

Ten gm Albendazole was poured gently through a glass funnel in to a 50ml graduated cylinder. The cylinder was tapped on a mechanical tapper apparatus until a constant volume was obtained. Volume occupied by the sample after tapping was recorded and tapped density was calculated using **eq no. 3.1.** The tapped density is found to be **0.33gm/ml.**

4.3.2 Bulk density

Ten gm of powder of Albendazole was taken and poured in the measuring cylinder and its volume was measured accurately and bulk density was calculated using **eq no.3.2.** The bulk density of Albendazole is found to be **0.22gm/ml.**

4.3.3 Hausner's ratio

It is the ratio of tapped density to the bulk density. It provides an indication of the degree of densification which could result from vibration of the feed hopper.it was calculated using **eq.no. 3.3.** The hausner's ratio of Albendazole is found to be **1.5 .** It indicates the very poor flow ability.

4.3.4 Flow property (Angle of repose)

Angle of repose was determined using fixed funnel method. The blend was poured through a funnel that was raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose was calculated using **equation.no. 3.4**. The angle of repose of Albendazole is found to be **41.38°.** It indicates the very poor flow ability.

4.3.5 Solubility

The solubility of albendazole was determined by using different solvent and the results are summarized in

Table 4.2.

Table 4.2: solubility profile of albendazole

Chemicals	Properties (Soluble/Insoluble)
Water	Insoluble
Chloroform	Soluble
Methanol	Soluble
Ethyl Acetate	Soluble

4.4 Post Formulation Evaluation

All the formulated batches of albendazole candies were evaluate for various test parameters.

4.4.1 Weight Variation

Twenty candies were selected randomly from each formulation, weighed individually and the weight variation was determined and the datas are tabulated in **Table No. 4.3** and also shown in **Figure No. 4.3**. Among the nine formulations it was found that the formulation F1 had a minimum weight whereas formulation F9 had a maximum weight. It was observed that weight variation of all the formulations ranged within the limit.

Table No. 4.3: weight variation(gram)

S.No	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	5.172	5.2012	5.2291	5.2531	5.2872	5.3074	5.3428	5.3593	5.3842
2	5.183	5.231	5.2231	5.2523	5.2874	5.3076	5.3546	5.3598	5.3847
3	5.148	5.234	5.2345	5.2534	5.2845	5.30734	5.3423	5.345	5.452
4	5.124	5.231	5.2213	5.2543	5.2819	5.3078	5.3421	5.354	5.463
5	5.213	5.243	5.2234	5.2532	5.2865	5.3078	5.3456	5.357	5.5237
6	5.214	5.241	5.2265	5.2412	5.2856	5.3075	5.3424	5.3287	5.3596
7	5.174	5.251	5.224	5.2561	5.2786	5.3075	5.3465	5.3597	5.3845
8	5.184	5.2543	5.2254	5.2543	5.28534	5.3079	5.3435	5.3596	5.2894
9	5.178	5.231	5.2231	5.2452	5.2856	5.3075	5.34765	5.35978	5.3895
10	5.147	5.2313	5.2234	5.2523	5.2834	5.3076	5.34561	5.3596	5.3785
11	5.176	5.213	5.123	5.2543	5.28765	5.3079	5.34123	5.3595	5.36574
12	5.175	5.231	5.2315	5.2512	5.28453	5.3075	5.3435	5.35945	5.3756
13	5.1783	5.242	5.2134	5.2543	5.28765	5.3078	5.3476	5.3597	5.452
14	5.183	5.235	5.2341	5.2541	5.28654	5.3074	5.3463	5.3586	5.673
15	5.1762	5.2421	5.2312	5.2513	5.2897	5.30732	5.3425	5.35954	5.4523
16	5.1723	5.232	5.2132	5.2531	5.28453	5.3076	5.3425	5.35963	5.5432
17	5.176	5.2723	5.2123	5.2564	5.28342	5.30746	5.3543	5.3597	5.4563
18	5.179	5.2713	5.2341	5.2546	5.2876	5.3087	5.362	5.3596	5.3564
19	5.145	5.273	5.2134	5.2316	5.2876	5.30745	5.3463	5.3598	5.4567
20	5.1756	5.2134	5.2132	5.2523	5.2876	5.30786	5.34527	5.3576	5.3498
AVG	**5.17324**	**5.24121**	**5.21783**	**5.25129**	**5.28546**	**5.30766**	**5.34595**	**5.35647**	**5.42451**
S.D	**0.02026**	**0.01857**	**0.02312**	**0.00569**	**0.00246**	**0.0003**	**0.00508**	**0.00725**	**0.08312**
MIN.	**5.124**	**5.2012**	**5.123**	**5.2316**	**5.2786**	**5.30732**	**5.34123**	**5.3287**	**5.2894**
MAX.	**5.214**	**5.273**	**5.2345**	**5.2564**	**5.2897**	**5.3087**	**5.362**	**5.3598**	**5.673**

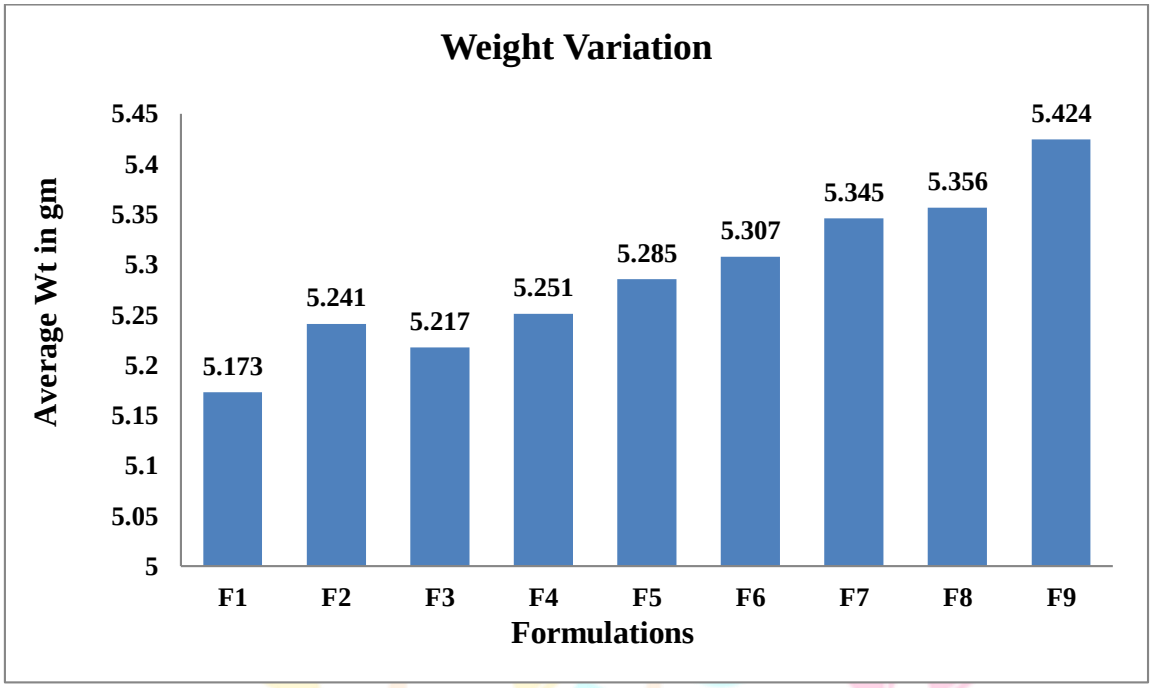

Figure 4.3: weight variation of different formulations of albendazole

4.4.2 Drug content uniformity

The result of Content uniformity is presented in **Table No. 4.4** and **Fig.No.4.4**. According to the result , formulation F2 has maximum drug content of 98.328% and formulation F5 has minimum drug content of 97.179% . The overall drug content ranges from 97.179% to 98.328% in nine formulations. Also, from the obtained results it is clear that content uniformity is within the limit.

Table No. 4.4: assay of different formulation

S.No.	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	97.4567	96.26866	96.1194	96.86567	95.67164	95.37313	97.9567	96.26866	95.8209
2	96.56716	98.35821	96.41791	99.40299	95.97015	95.8209	98.95522	95.8209	96.41791
3	96.86567	96.86567	96.86567	96.1194	96.86567	96.41791	98.50746	95.8209	98.95522
4	98.35821	97.31343	98.95522	97.76119	96.41791	96.86567	97.16418	98.95522	95.97015
5	97.91045	97.46269	100.2985	99.85075	96.1194	97.16418	98.95522	98.35821	97.01493
6	98.50746	98.50746	95.8209	98.50746	98.35821	96.56716	95.97015	98.95522	98.50746
7	98.80597	98.65672	97.16418	95.67164	97.16418	98.35821	96.26866	95.8209	99.40299
8	98.95522	97.76119	98.50746	96.26866	95.97015	98.50746	97.31343	98.65672	98.80597
9	98.35821	98.95522	99.85075	96.86567	98.35821	99.40299	98.65672	98.65672	98.65672
10	99.85075	98.65672	98.65672	97.01493	98.80597	97.91045	98.95522	96.41791	95.97015
11	95.97015	98.35821	99.40299	96.41791	96.56716	100.1493	96.86567	98.80597	99.25373
12	97.16418	99.40299	100.7463	95.8209	97.01493	99.55224	95.37313	100.1493	98.95522
13	96.41791	100.7463	98.95522	97.31343	97.46269	100.4478	100.2985	99.25373	95.8209
14	98.50746	98.80597	97.46269	96.56716	97.76119	95.97015	98.80597	95.67164	97.16418
15	95.8209	98.50746	98.35821	98.65672	98.35821	100.7463	99.10448	98.50746	97.46269
16	96.56716	98.95522	98.80597	95.52239	96.41791	98.65672	95.67164	100.7463	98.50746

17	98.65672	97.76119	97.76119	95.67164	97.31343	96.41791	100.7463	96.1194	97.76119
18	96.26866	98.65672	98.35821	95.97015	98.65672	100.4478	98.65672	95.52239	96.1194
19	96.86567	97.61194	96.41791	100.8955	98.95522	98.80597	100.4478	95.97015	95.8209
20	98.65672	98.95522	98.50746	98.0597	95.37313	96.41791	97.46269	98.65672	97.31343
AVERAGE	**97.6266**	**98.3284**	**98.1716**	**97.2612**	**97.1791**	**98**	**98.1068**	**97.6567**	**97.4851**
S D	**1.13761**	**0.95172**	**1.35884**	**1.49274**	**1.09159**	**1.69283**	**1.52483**	**1.65065**	**1.27808**
MIN	**95.8209**	**96.2687**	**95.8209**	**95.5224**	**95.3731**	**95.3731**	**95.3731**	**95.5224**	**95.8209**
MAX	**99.8507**	**100.746**	**100.746**	**100.896**	**98.9552**	**100.746**	**100.746**	**100.746**	**99.403**

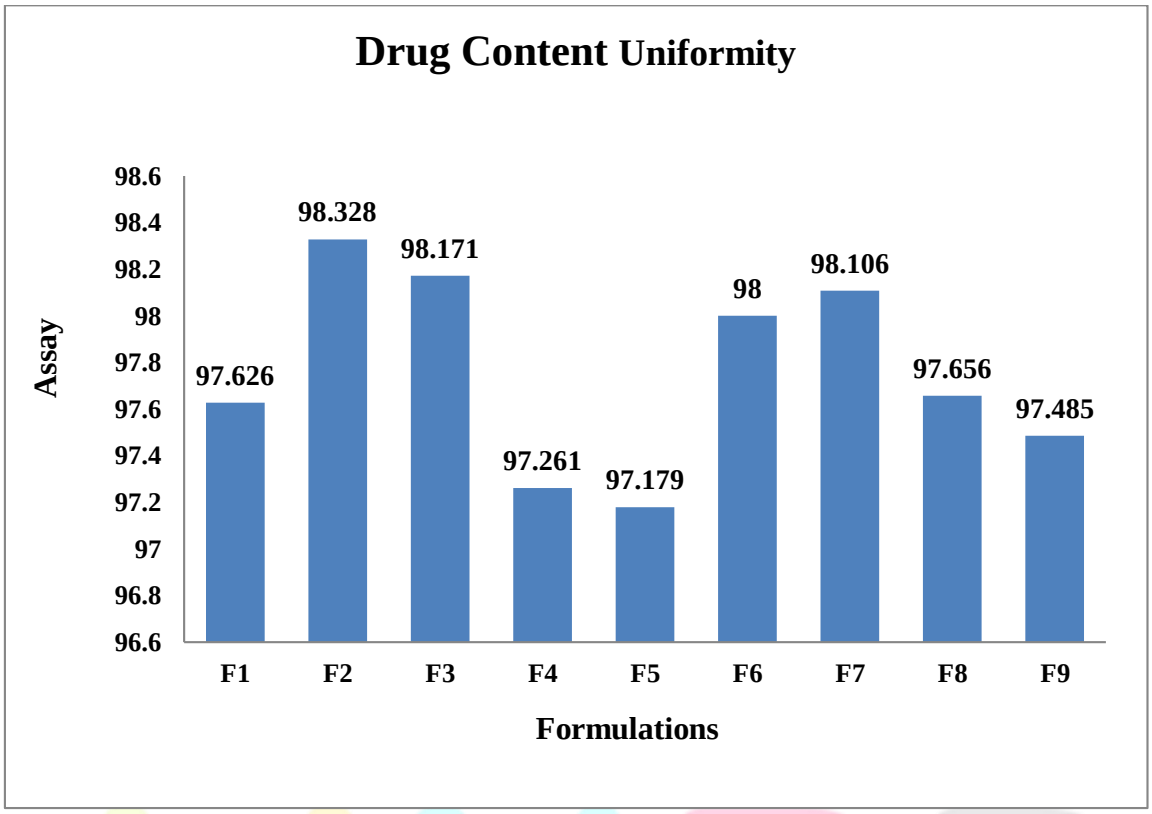

Figure 4.4: drug content uniformity of different formulations of albendazole

4.4.3 Dissolution test

The dissolution test of different formulation of albendazole candies were performed. Cumulative percentage drug release from the different formulation of albendazole is shown in **Fig No.4.5** and the obtained data is presented in **Table No. 4.5** which shows the drug release from all the formulation is within the limit.

The data obtained from the dissolution is fitted in different mathematical models (zero, first order release kinetics). The drug release from the medicated candies is best described by zero order kinetics with maximum R^2 values as shown in **Table No. 4.6**. Comparing the cumulative % drug release (98.10127) and R^2 value (0.996) it was found that the formulation F5 shows the better drug release from the candies. The drug release is higher in formulation using 4% glycerine with gelatin was described in some article[Nwakile C.D, Onunkwo G.C, Osonwa U.E, Umeyor C.E, Uronnachi E.M, and Emesih O.C,2012].

The dissolution data are analyzed by using model independent model ie. similarity and dissimilarity factor. From the result it is clear that the drug release from the nine formulations are highly similar. As the similarity factor (f_2) for all the formulations are near to 100 and the dissimilarity factor (f_1) are below 15 as shown in **Table No. 4.7.**

Table No. 4.5: dissolution of different formulation

Formulation/ Time(Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
15	62.41712	62.56781	64.13502	63.17058	56.36769	54.58107	60.78963	59.22242	57.80591
30	75.01507	73.99036	73.89994	73.59855	68.10549	72.30259	73.38758	71.69982	72.27245
45	82.1729	82.54973	82.24834	82.54973	82.54973	82.91139	82.61001	82.27848	79.11392
60	94.93671	91.0711	96.08198	95.81073	98.10127	92.91742	92.24352	97.32851	95.75045

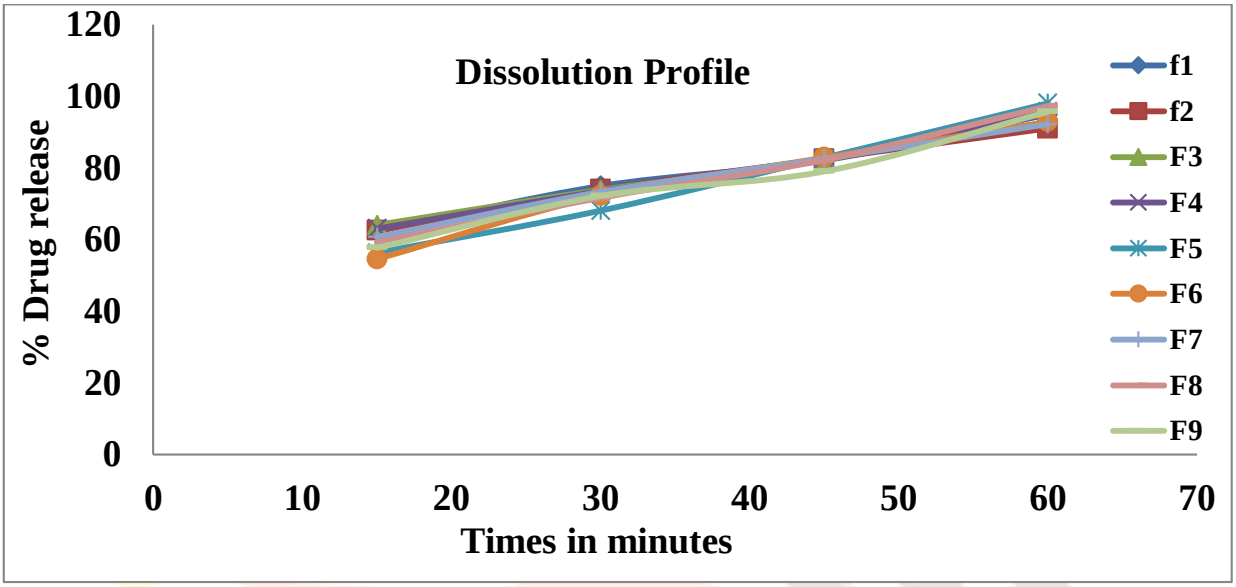

Figure 4.5: Dissolution Profile of Different Formulations of Albendazole

Table 4.6: release kinetics of albendazole candy

Formulation	Zero Order Kinetics R^2	First Order Kinetics R^2
F1	0.989	0.897
F2	0.994	0.9768
F3	0.988	0.8571
F4	0.993	0.8753
F5	0.996	0.84
F6	0.978	0.9757
F7	0.994	0.9655
F8	0.995	0.8479
F9	0.978	0.8515

Table 4.7: similarity and dissimilarity factor

Formulation	Similarity Factor (f2)	Disimilarity Factor (f1)
F1 vs F2	85.62	1.49
F1 vs F3	90.59	1.29
F1 vs F4	93.20	1.09
F1 vs F5	83.49	1.78
F1 vs F6	67.84	4.23
F1 vs F7	90.09	1.39
F1 vs F8	79.95	2.23
F1 vs F9	74.26	3.57

CHAPTER V

CONCLUSION AND RECOMMENDATION

5.1 Conclusion

Albendazole is a broad-spectrum anthelmintic(Agents that kill parasitic worms). It is widely used for the management and treatment of intestinal nematode infection. It is also quite effective as a single-dose-treatment for ascariasis, hookworm infections, and trichuriasis. Albendazole is practically insoluble in water but slightly soluble in solvents like chloroform, methanol, ethyl acetate, and acetonitrile.

The preformulation evaluation of Albendazole powder i.e tapped density, bulk density, hausner's ratio, angle of repose were evaluated. Nine batches of Albendazole candy were formulated using albendazole sucrose, dextrose, methyl cellulose, citric acid and glycerin.

Post formulation evaluation includes weight variation, drug content uniformity and dissolution were evaluated. Weight variation and drug content uniformity were within the limit. Although the drug release pattern is almost similar in all the formulation, comparing the cumulative % drug release and R^2 value it was found that the formulation F5 shows the better drug release from the candies among all.

5.2 Recommendation

- The research can be carried out so as to find out the stability of albendazole at 90°C
- The weight of candy can be decreased using appropriate mould size so as to make it acceptable size for paediatrics.
- The research can be carried out in a controlled environment so that various environmental factors like humidity, moisture, temperature affecting the research are stabilized.
- Stability testing can be performed.
- Forced degradation study can also be performed.

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