ISSN 2349-7823

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org

FORMULATION AND EVALUATION OF ANTHELMINTIC HERBAL SUPPOSITORY CONTAINING THE COMBINATION OF LEAF EXTRACTS OF *Quassia indica and Vitex negundo*

Dr. Syed Asadulla[1*], Alan Jacob[2*], Dr. Ajit Babu[3], Alufath shahza[4], Moosan basil kallatra[5], Sajana[6], Shijina Shibu[7]

[1]Professor, [2]Associate Professor, [3]principal, [4, 5, 6, 7, (]Research coordinates), Department of Pharmacognosy, Malik Deenar College of Pharmacy, Seethangoli, Bela (P.O), Kasaragod, India.

Corresponding author: Mr. Alan Jacob, Dr. Syed Asadulla

DOI: https://doi.org/10.5281/zenodo.7491379

Published Date: 29-December-2022

Abstract: **The plants such as *Quassia indica* and *Vitex negundo* showed anthelmintic property. In this work aqueous leaf extracts of *Quassia indica* and *Vitex negundo* were combined and formulated into a suppository. Suppositories are inserted directly into the rectum to distribute their active constituent to internal areas. It is used as anthelmintic for helminthiasis. Extraction was done by maceration technique using chloroform water as solvent. Moulding was used for the preparation of suppositories, which were evaluated for their physicochemical properties and in vitro drug release characteristics. Suppositories which contain polyethylene glycol (PEG) 4000 and surfactant tween 80 showed better permeation of drug and action.**

***Keywords:* *Quassia indica*, *Vitex negundo*, Maceration, Suppository, PEG 4000, Tween 80.**

1. INTRODUCTION

Helminths have plagued humans since before the era of our earliest recorded history. The eggs of intestinal helminths can be found in the mummified feces of humans dating back thousands of years, and we can recognize many of the characteristic clinical features of helminth infections from the ancient writings of Hippocrates, Egyptian medical papyri, and the Bible. Helminthiasis causes a significant health problem with increased morbidity and, to some extent, mortality in an underdeveloped and developing country, although it may also occur in developed countries. It remains undiagnosed in many patients, and they suffer a lot due to many complications. This activity reviews the evaluation and treatment of helminthiasis and highlights the role of the interprofessional team in evaluating and treating patients with this condition. In developing countries, the most common infectious agents of humans are these helminthic infections. More than a quarter of the world's population, that means approximately 2 billion people are affected by the helminthic parasite, and it is one of the major burdens of developing countries, especially in children. [1-7]

According to WHO, Standardization and Quality Control of herbals is the process involved in the physicochemical evaluation of crude drug covering aspects. Herbal formulations are pharmaceutical dosage forms prepared from parts like leaves, roots, rhizomes, wood, bark, fruits, seeds, corms, flowers, and flowering buds used to cure diseases. Conventionally, herbal dosage forms are of two types; Ayurvedic dosage forms (churna, bhasma, lepa etc.) and modern dosage forms

(tablets, capsules, ointments, suppositories etc). The process of evaluating the drug quality and purity by various parameters like morphological, physical, chemical, biological parameter etc. is called standardization.[8]

The term **anthelmintic** is restricted to drugs acting locally to expel parasites from GIT, these are drugs which are used to treat parasitic infestation due to flat worm and round worms. They act either locally to expel worms from GIT or systematically to eradicate species and developmental forms of helminths, which invade organs and tissues. Helminthes parasitic to human and other animals are derived from two phyla, platy helminths (flatworm) and nemathelminths (roundworms). Worm infestation is one of the major global public health problems, more so in tropical countries. Besides the environmental condition peculiar to tropics, poverty, illiteracy, lack of adequate sanitary facilities and of pure water supply make total eradication of this Problem. The commonest parasites observed are roundworms, hookworms, threadworms, tapeworms, filarial worms, and guinea worms.[9]

Herbs such as ***Quassia indica* and *Vitex negundo*** belonging to Simaroubaceae and Verbenaceae family, is traditionally used for the conditions such as anthelmintic, anorexia, indigestion, constipation, and fever.

Suppositories are designed for insertion into body cavities where they melt, soften, or dissolve and exert local or systemic effects. The suppositories serve as an alternate where oral administration of drug is not suitable as in infants or patients suffering from nausea, vomiting and gastrointestinal disturbances. They provide the advantage that biotransformation of drugs in liver, pH conditions and gastrointestinal enzymes are avoided. The suppository base play vital role in the release of medicament they hold the drug. The important property of suppository base is that it should remain solid at room temperature but soften, melt or dissolve readily at body temperature so that the drug is released after its administration.

The **advantage** of this rectal suppositories is to reduce biotransformation in the liver can also prevent destruction by intestinal enzymes or pH in the stomach and can make it easier for people with intestinal worms that are difficult to swallow the drug. So that the aim of this study was to formulate a suppository by combining leaf extracts of *Quassia indica* and *Vitex negundo.* [10,11]

2. MATERIALS AND METHODS

Plant collection and authentication

The leaves of *Quassia indica* and *Vitex negundo* was collected from the local region of Kasaragod district in Kerala and authenticated by Dr. Subrahmanyam Prasad K, Taxonomist, Nehru Arts and Science College, Kasaragod, Kerala, India.

Extraction

The powdered leaves, each weighed as 20 grams and then put into a macerator, then added 200 ml of aq. solvent (chloroform water) to each flask, until the powder is completely submerged. Let it stand for 3 x 24 hours, while stirring occasionally. Macerate is removed and accommodated, the filtrate obtained is mixed and then concentrated. [12]

Calibration of mould

Before preparing the suppositories, the mould should be calibrated because the moulds may vary in their capacity. The base was melted alone and then filled into the mould and weighed after removing the suppositories; the mean weight was taken as true capacity of the mould.[13]

Preparation of suppository

The suppositories bases were accurately weighed and melted on water bath. Finely divided drug powder was thoroughly incorporated in the melted base with continuous stirring. The melted mass was poured in the appropriate suppository mould. Suppositories were kept in refrigerator, to avoid the development of cracks and the exposure to room temperature was limited to less than 24hr before use in in vitro release studies. [14]

Evaluation of suppositories

Physicochemical Evaluation

Visual characterization: Two suppositories from each batch were randomly selected, longitudinally cut, and examined through naked eyes for the assessment of physical characters like absence of fissuring, pitting, fat blooming, exudation, and migration of active ingredients.

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org

Length and width: Six suppositories were selected randomly from each batch; their length and width were measured using Vernier callipers.

Weight variation: Six suppositories were weighed and average weight was calculated. Each suppository was weighed individually on electronic balance. No suppositories should deviate from average weight by more than 5% except two which may deviate not more than 7.5%.[15]

Melting point: Macro melting range test was performed with the whole suppository. Suppository from each formulation was placed in a test tube with phosphate buffer pH 7.2 maintained at constant temperature 37±0.5°C. The time required by the whole suppository to melt or disperse in the media was noted. The melting time plays a crucial role in the release of active ingredient.

Liquefaction: Liquefaction time was measured using a burette having a broad opening on one side and a narrow opening on the other suppository was pushed inside form the broad end side to reach to the narrow end. 5ml of phosphate buffer pH 7.2 was placed inside the burette, maintained at 37±0.5°C. A thin glass rod was placed on the top of the suppository and the time at which the glass rod just inserts into the suppository was recorded as liquefaction time. This indicates the time taken by the formulation to liquefy under similar pressures found in rectum.[16]

Disintegration test: The disintegration time of the suppositories was performed by using disintegration test apparatus. The time taken for the disintegration of entire suppository was recorded. Phosphate buffer pH 7.2 maintained at 37±0.5°C was used for this testing.[17]

Hardness (fracture point): Hardness of the prepared suppositories was tested using Monsanto hardness tester model. The weight required for suppository to collapse was taken as measure of hardness of the suppository. Hardness test or fracture point test was carried to determine the tensile strength of the suppositories to access whether they will be able to withstand the hazards of packing and transporting.[18]

Pharmacognostical evaluation

Determination of extractive values: This method determines the number of active constituents in each amount of plant material when extracted with solvent. The extractive value is used as a means of evaluating crude drug which are not readily estimated by other means.

• **Alcohol soluble extractive value**

5 grams of each suppository formulation taken with 100 ml ethanol in a stoppered flask for 24 hours with occasional shaking during the first 6 hours and allowed to stand undisturbed for another 18 hours. Filtered rapidly, by taking precautions against loss of alcohols. The 25 ml of the filtrate was evaporated to dryness in a tared bottomed shallow dish, dried at 105°C and weighed. Calculated %w/w ethanol soluble extractive with reference to air dried material.

• **Water soluble extractive value**

In a conical flask, 5 g of suppository added with 100 ml water for 1 day, shaking after every 6 hours and filtered. Evaporated 25 ml of filtrate in Petri dish at 105°C and weighed the solid matter.

• **Petroleum Ether soluble extractive value**

5 grams of each suppository formulation taken with 100 ml Petroleum ether in a stoppered flask for 24 hours, with occasional shaking during the first 6 hours and allowed to stand undisturbed for another 18 hours. Filtered rapidly, then 25 ml of the filtrate was evaporated to dryness in a tarred flat bottomed shallow dish, dried at 105^0C and weighed. Calculated %w/w ether soluble extractive with reference to air dried material.

Determination of ash value

The ash value is an important parameter for the evaluation of crude drugs, due to variation of values within wide limit. The ash value of any organic material is composed of inorganic material like metallic salt and silica.

The following three methods were developed

Total ash

Acid insoluble ash

Water soluble ash

Ashing involves an oxidation of the component of the product and a high ash value involves the contamination, substitution, adulteration, or carelessness in the preparation of crude drug for marketing.

• Total ash

2 grams of each suppository was weighed out in a crucible previously ignited for 30 minutes, spread evenly, and ignited at a temperature of not more than 450^0C until it showed no signs of carbon, then cooled in the desiccator and weighed. Calculated the content of total ash per gram of air-dried material.

• Acid insoluble ash

The crucible containing the total ash was filled with 25 ml of 2N HCI, covered with watch glass, and boiled gently for 5 minutes. The watch glass was rinsed with 5 ml of hot water and then added into the crucible. Collected the insoluble matter on an ash-less filter paper and washed with hot water until the filtrate was neutral. Filter paper containing the insoluble matter was transferred to the original crucible, dried on a hot plate, and ignited to constant weight. The residue was allowed to cool in a desiccator for 30 minutes, then weighed, calculated the content of acid insoluble ash per gram of air-dried material.

• Water soluble ash

To the crucible containing the total ash, 25 ml each of water was added and boiled for 5 minutes. The insoluble matter was collected in sintered glass crucibles. Washed with hot water and ignited at a temperature not exceeding 450°C. The weight of those residue in mg was subtracted from the weight of total ash. The content of water-soluble ash was calculated per gram of air-dried material.[19]

Determination of Acid value

5gm of the suppository was weighed and dissolved in 25ml of equal volume of Petroleum ether and ethanol, previously neutralized with 0.1N potassium hydroxide by using phenolphthalein as indicator. Shake well and dissolved in 1ml of phenolphthalein and titrated with 0.1N of potassium hydroxide solution until permanent pink colour formed.[20]

Drug Content

Determination of the drug content, the suppositories were dissolved in 100 ml phosphate buffer of pH 7.4 by stirring through magnetic stirrer slowly at 37 °C for 1 hr.

After the solution was filtered; and the filtrate was diluted suitably and absorbance was measured against blank at 371nm.[21]

Measurement of pH

2 gm of suppository formulation was dispersed separately in 45 ml of water, and the pH of the suspension was determined using digital pH meter. Measurements of pH of all formulations were carried out in triplicate and the averages of three readings were noted.[22]

Dissolution Test

In vitro dissolution studies of suppositories were carried out in USP tablet dissolution test apparatus employing a rotating paddle apparatus (Type II) at 75 rpm and using 900 ml of phosphate buffer (pH 7.4) at 37±0.5 °C as dissolution medium. One suppository was used in each test. At pre-determined time intervals 10 ml sample were withdrawn by means of pipette then filtered through filter paper. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium and maintained at 37±0.5°C. The sample were analysed for drug release by measuring the absorbance at 320 nm using UV visible spectrophotometer.[23]

Drug diffusion study through egg membrane

Diffusion study was done by using Franz diffusion cell. The egg membrane was mounted between the donor and receptor compartments. Receptor compartments were filled with 15 ml of phosphate buffer maintained at 37^0C. 1 gm of each suppository were placed on the egg membrane, samples were withdrawn for a period of 10, 20, 30, 40, 50 and 60 min. The volume withdrawn at each interval was replaced with same quantity of fresh fluid to maintain sink condition. The withdrawn samples were analysed spectrophotometrically at 230 nm.[24]

ISSN 2349-7823

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org

Anthelmintic assay

Materials

Adult Indian earthworms (*Pheritima posthuma*) were collected from the moist soil of farm field (CPCRI, Kasaragod) and washed with distilled water to remove all the faecal matter, the earthworms of size 6-9 cm long and 0.1-0.2 cm wide were used in the experiments. 5 % DMSO and Albendazole (50mg/ml,100mg/ml) were used as control and std drug respectively in the study.

Assay

Anthelmintic activity was evaluated by exposing the adult *Pheritima posthuma* to 2 different concentrations of anthelmintic suppository of *Quassia indica* and *Vitex negundo*. The anthelmintic activity was performed according to the method of Ghosh et al. with slight modifications. The suppositories were dissolved in minimum amount of DMSO (5%) and then volume is adjusted to 10 ml with distilled water. 10 ml of formulation containing two different concentrations (10% and 20%) of each of the suppository were prepared and 6 worms (same type) were placed in the petri dishes. The std drug and extract solutions were prepared freshly before starting the experiment. Time for paralysis was noted when no movement could be observed except when the worms were shaken vigorously. Time for death of worms were recorded after sometime that worms neither moved when shaken vigorously nor when dipped in hot water (50°C) followed by fading away of their body colours. Albendazole (50mg/ml, 100mg/ml) was used as reference standard.[25]

Stability studies

Short term stability studies were performed at a room temperature and refrigeration temperature was kept for 4 weeks on the promising formulation. The suppositories were individually wrapped in aluminium foil and packed in cardboard boxes. Sample is taken after 4 weeks and estimated for physical appearance and pH. [23]

3. RESULTS AND DISCUSSIONS

Plant collection

The collected materials were cleaned to remove the adhered dust particles and were then dried in shade at room temperature. The dried plant materials were coarsely powdered, weighed, and stored in an air tight container till use.

Extraction

Table no: 1 Percentage yield of aqueous leaf extracts of *Quassia indica* and *Vitex negundo*

Sl no	Herbs	Amount of drug powdered (g)	Amount of extract obtained (g)	Percentage yield (%w/w)
1	Quassia indica	20	0.42	2.15
2	Vitex negundo	20	0.37	1.85

Preparation of suppository

2 formulations of suppositories containing 10% and 20% of aq. extract of *Quassia indica & Vitex negundo* was prepared

Formulation-I

Table no: 2 Formulation-I

Ingredients	Contents (gm)
Plant extracts	0.8
PEG 4000	7.12
Tween 80	0.8

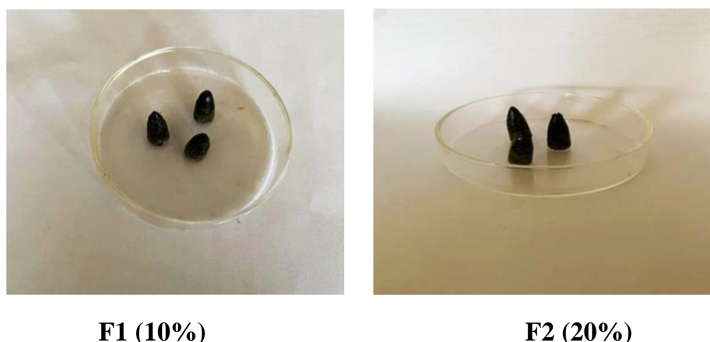
Formulation-II

Table no: 3 Formulation-II

Ingredients	Contents (gm)
Plant extracts	1.6
PEG 4000	7.05
Tween 80	0.8

ISSN 2349-7823

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org



F1 (10%) **F2 (20%)**

Fig no: 1 Suppositories containing two different concentrations of drug

Physicochemical evaluation

Table no: 4 Results showing physicochemical characterization of the suppository formulations

Parameters	**F1**	**F2**
Fissuring	No	No
Pitting	No	No
Fat blooming	No	No
Exudation	No	No
Migration of ingredient	No	No
Length (cm)	2.13	2.22
Width (cm)	1.11	1.12
Weight variation (%)	1.81±0.11	1.99±0.11
Melting time (min)	35.03±0.4	45.3±0.24
Hardness (kg/cm^2)	3.01±0.18	2.8±0.11
Liquefaction (min)	11.72±0.34	11.21±0.05
Disintegration (min)	9.26±0.024	10.1±0.038
Drug content (%)	96.24	99.45

Pharmacognostical studies

Table no: 5 Results showing Pharmacognostical studies of the suppository formulations

Sl no	**Parameters**	**Formulation**	**Average (%W/W)**
1	Water soluble extractive	F1	1.09
		F2	0.58
2	Alcohol soluble extractive	F1	1.22
		F2	1.30
3	Ether soluble extractive	F1	0.97
		F2	1.03
4	pH	F1	7.4
		F2	7.6
5	Acid value	F1	0.67
		F2	1.23
6	Total ash	F1	1.10
		F2	1.73
7	Water soluble ash	F1	0.59
		F2	0.91
8	Acid insoluble ash	F1	0.67
		F2	1.09

ISSN 2349-7823

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org

Dissolution studies

The dissolution study showed that the suppositories melted in the dissolution medium maintained at 37±0.5 ^{0}C. The in vitro drug release profile of suppositories.

Table no: 6 Mean cumulative percentage drug release

TIME INTERVAL (min)	F1(10%)	F2(20%)
10	78.5	67.25
20	81.875	72.875
30	86.93	76.81
40	88.62	84.25
50	90.875	87.34
60	90.894	87.375

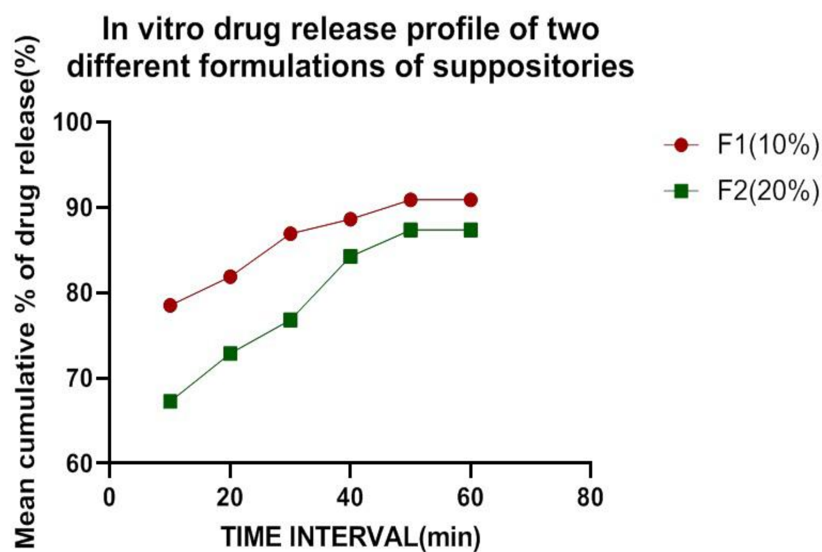


Fig no: 2 Drug release profile of both F1 and F2 formulations by using dissolution study

Drug diffusion study

Table no: 7 Percentage drug release of F1 and F2 formulations

Time (min)	**Drug release**	
	F1 (%)	**F2 (%)**
10	76.90	69.70
20	82.03	74.20
30	86.21	76.90
40	89.30	83.80
50	90.98	88.06
60	91.05	88.94

ISSN 2349-7823
International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org

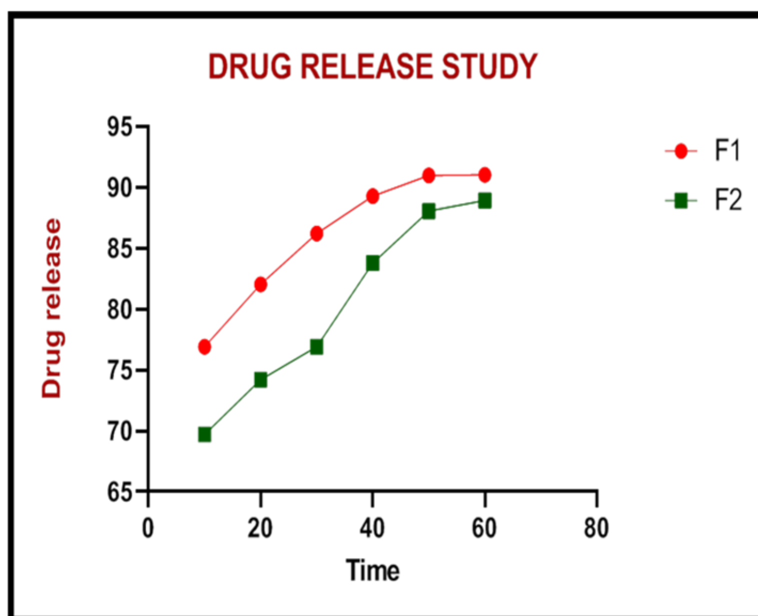


Fig no: 3 Drug release profile of both F1 and F2 formulations by using diffusion method

Anthelmintic assay

Table no: 8 Anthelmintic activity of suppository containing aqueous leaf extracts of *Quassia indica* and *Vitex negundo*

Sl no	F1		F2		Standard (Albendazole)	
	Paralysis time (min)	Death time (min)	Paralysis time (min)	Death time (min)	Paralysis time (min)	Death time (min)
1	7.45	8.21	6.89	7.68	7.84	8.13

The anthelmintic studies were conducted for both the formulations F1 and F2. Results were compared with standard albendazole. DMSO was used as control. Both the formulations show potent anthelmintic activity than standard.

Stability studies

Stability studies showed that there was no significant change in drug content, physical character, and pH of suppositories after storing them 4 weeks at refrigeration and room temperature. The changes in the physical parameters of F1 was observed after 30 days. It showed refrigeration storage is better than room temperature for suppository's storage.

Table no: 9 Result showing stability studies of formulations

Sl no	Day	Formulation	Temperature	pH	Appearance
1	After 30 days	F1	Room temperature Refrigeration	7.2 7.2	No colour change No colour change
2	After 30 days	F2	Room temperature Refrigeration	7.4 7.4	No colour change No colour change

4. CONCLUSION

Leaves of the herbs *Quassia indica* and *Vitex negundo* were taken, dried and powdered. Extraction of dried powder of the drug was done by maceration using chloroform water as solvent. Aqueous extracts of leaves of the plant *Quassia indica* and *Vitex negundo* were formulated as herbal suppository by using suitable base such as PEG 4000 and surfactant tween 80. Prepared formulations were evaluated for various physico chemical parameters such as color, pH, liquefaction, hardness, melting point, disintegration, and weight variation. Pharmacognostical evaluations and anthelmintic assay were also carried out, and all the tests showed satisfactory results. As per the studies and obtained results, the aqueous extract of leaves of the plant *Quassia indica* and *Vitex negundo* can be successfully formulated into herbal suppository. Both the formulation has good dissolution property, while formulation 1 has better drug release rate than formulation 2.

Both the formulations are in the pH range of 7.4 – 7.6, which is like rectal pH, hence these suppositories found to be compatible with rectal pH. All the suppositories showed 50% of drug release within 10 min, this is due to the addition of surfactant tween 80. Based on the in vitro release rate studies, it can be concluded that polyethylene glycol 4000 can be used as a base which were easily soluble in aqueous medium, disperses rapidly and has higher rate of drug release for immediate release of herbal suppositories. The drug is compatible with excipients such as base and surfactant, so the formulation can be readily prepared. From the study, we can conclude that F1 formulation shows greater anthelmintic, better drug release and good dissolution property.

REFERENCES

[1] Cox F.E.G. History of human parasitology. Clin. Microbiol. Rev. 2002;15:595–612.

[2] Hotez P.J., Ottesen E., Fenwick A., Molyneux D. The neglected tropical diseases: the ancient afflictions of stigma and poverty and the prospects for their control and elimination. Adv. Exp. Med. Biol. 2006;582:23–33.

[3] Hotez P.J. Forgotten people and forgotten diseases, the neglected tropical diseases and their impact on global health and development. ASM Press. 2008;4(1): 43-47.

[4] Hotez PJ, Brindley PJ, Bethony JM, King CH, Pearce EJ, Jacobson J. Helminth infections: the great neglected tropical diseases. J Clin Invest. 2008;118(4):1311-21.

[5] Jourdan PM, Lamberton PHL, Fenwick A, Addiss DG. Soil-transmitted helminth infections. Lancet. 2018;391(10117):252-265.

[6] Novianty S, Dimyati Y, Pasaribu S, Pasaribu AP. Risk Factors for Soil-Transmitted Helminthiasis in Preschool Children Living in Farmland, North Sumatera, Indonesia. J Trop Med. 2018; 201(8):6706413-419.

[7] Samuel F, Demsew A, Alem Y, Hailesilassie Y. Soil transmitted Helminthiasis and associated risk factors among elementary school children in ambo town, western Ethiopia. BMC Public Health. 2017;17(1):791.

[8] Folashade O, Omoregie H, Ochogu P, Standardization of herbal medicines-A review. International Journal of Biodiversity and Conservation, 2012; 4(3): p. 101-112.

[9] Gupta P. J., European review for medical and pharmacological sciences, 2007; 3(11): p. 165-170.

[10] Aulton ME, Wells TI. Pharmaceutics, The science of dosage form design, London, 1998; 1(2): p. 218-220.

[11] Jannin V, Lemagnen G, Gueroult P, Larrouture D, Tuleu. Rectal route in the 21st Century to treat children Drug Delivery Rev, 2014; 1(73): p. 34-49.

[12] Wilson and Gisbold's Textbook of organic medicinal and pharmaceutical chemistry, 2012; 12(11): p. 264-265.

[13] Loyd V. Allen, "Quality control of suppositories" in suppositories pharmaceutical press, London, 2008; 7(2): p. 141-142.

[14] Hammer M.-L.-A. and Johns E.-A. -Amazonian plethora: four medicinal plants of Marajo mat, 1993; 10(1): p. 241-244.

[15] El-majri M. Sharma RK. Formulation and evaluation of piroxicam suppository. International journal of drug delivery, 2010; 1(2): p. 108-112.

[16] The ayurvedic pharmacopoeia of India, Delhi; The controller of publications, 1999; 1(2): p. 190-191.

[17] Saleem MA. Taher M. Sanaullah S. Formulation and evaluation of tramadol hydrochloride rectal suppositories. International journal of pharmaceutical science, 2008; 2(5): p. 641-645.

[18] Gowthamarajan K. Venketeshwaran G. Suresh B, Formulation and evaluation properties of meloxicam solid dispersion incorporated suppositories. Indian journal of pharmaceutical science, 2002; 2(4): p. 525-528.

[19] Mishra Manisha U, Journal of advanced science research, 2013; 4(3): p. 37-40.

[20] Pugunes S., International journal of pharmaceutical science and research, 2013; 4(2): p. 617-621.

ISSN 2349-7823

International Journal of Recent Research in Life Sciences (IJRRLS)
Vol. 9, Issue 4, pp: (16-25), Month: October - December 2022, Available at: www.paperpublications.org

[21] Varshney Himanshu M, Asian journal of pharmaceutical and clinical research, 2012; 5(4): p. 235-238.

[22] Bag G C, Devi P G, Bhaigyabati, Phytochemical screening and antioxidant activity of *Meyna laxiflora*. Int. J. Pharm. Sci. Rev, 2016; 36(1): p. 137-143.

[23] Yousif HS, Formulation of tinidazole rectal suppositories. Asian journal of pharmaceutical sciences, 2011; 10(2): p. 69-83.

[24] Prasanna sundaripingali, prathimasrinivas, B. Madhava Reddy: Miconazole loaded novel phytosomal topical gels, WJPPS, 2015; 4(10): p. 2305-2320.

[25] Palaksha MN, Evaluation of in vitro antibacterial and anthelmintic activities of *Sauropus androgynus* (Phyllanthaceae) plant extracts. Int J Pharmacognosy chinese med, 2019; 3(2): p. 160-162.