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Worm Infestation and child health care: Anthelmintic Pellets of Papaya

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ABSTRACT: Backgrounds: Papaya seeds are claimed to possess anthelmintic property in traditional systems of medicine. But because of its bitter taste it leads to patient non compliance. Taste is a critical factor to be considered while formulating oral dosage forms. The present study revealed that the powder layering technique of pelletization is one of the most valuable technology of taste masking in the preparation of oral dosage forms. **Aim:** The research study was aimed to prepare and evaluate the Pellets containing papaya seed loadings in microbial triggered polymer for anthelmintic activity. **Methods:** The papaya seeds were extracted with 100 ml 70 % aqueous methanol by Soxhlation method. The seed extracs were evaluated for physical and chemical tests. The papaya pellets was prepared by extrusion spheronization method. The pellets were coated with amino acid as a taste masking agent. The pellets were evaluated for size, shape, density, flow property, friability, disintegration and in vitro dissolution studies. The taste masking of processed formulation was evaluated *in vitro* by dissolution method and chromatographic technique, while anthelmintic effect was evaluated by using six adult Indian earthworms and cattle worms. **Results:** The result of present study indicated that the Papaya seeds lead to paralysis of earthworm and death after some time. **Conclusion:** Thus, the present study demonstrated that the Papaya seed is a potent anthelmintic.

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Key words: Anthelmintic, papaya seed extract, pelletization, spheronization.

INTRODUCTIONS:

The World Health Organization estimates that a staggering two billion people harbour parasite worm infections. Development of resistance to most of the commercially available anthelmintics became a severe problem worldwide [1]. Moreover, these drugs are unaffordable, inaccessible or inadequately available to the poor peoples in developing countries [2]. These factors paved the way for herbal remedies as alternative anthelmintics [3]. Screening and proper evaluation of the

claimed medicinal plants could offer possible alternatives that may be both sustainable and environmentally acceptable [4]. *Carica papaya* Linn. is a fast growing small tree, with straight, cylindrical, soft and hollow trunk roughened by the presence of large leaf and inflorescence scars. Papaya skin, pulp and seeds contain variety of phytochemicals. The seeds are black, tuberculous and enclosed in a transparent aril. The seeds are considered as carminative, emmemagogue, abortifacient, vermifuge, thirst quencher and counter irritant. Seed extract is used to treat bleeding piles and enlarged liver and spleen. Seed paste with glycerine can be applied to cure ringworm and psoriasis [5]. The ripe seeds are taken with rice and useful to treat diarrhoea. The seeds are effective to control diabetes mellitus, hypertension and hypercholesterolemia [6,7]. The papaya seed extracts showed antifertility effect, inhibited jejuna contraction and suppressed cauda epididymal sperm motility [8-10]. But the Papaya seed extract possess bitter taste which is highly unacceptable if using the oral route of delivery especially in case of pediatric drugs. However, for patients, such drugs are not necessarily easy to swallow, resulting in non-compliance and a subsequent decrease in efficiency. To overcome this problem various techniques have been developed to mask the unpleasant and bitter taste of drugs [11]. But in most cases, solid preparations are recommended for pediatric patients, instead liquid preparations are used. It is known that only dissolved substances elicit taste sensation and substances which are completely insoluble in water are tasteless [12].

Table 1. Formulation composition of anthelmintic herbal pellets.

Ingredients	PSP-01	PSP-02	PSP-03	PSP-04	PSP-05
Drug	25g pellets contain 10ml liquid Extract				
MCC	50	40	50	70	60
CTN	-	-	40	-	-
CRGN	20	30	-	-	-
SA	-	-	2.5	-	-
DCP	-	-	7.5	-	-
DXW	-	-	-	30	40
MNT	30	30	-	-	-
DW	q.s.	q.s.	q.s.	q.s.	q.s.

All values are expressed as %. MCC – Microcrystalline cellulose, CTN - Chitosan, CRGN – Caragennan, SA – Sodium alginate, DCP – Dibasic calcium Phosphate, DXW – Dextrin white, MNT – Mannitol, DW - Distilled water and q.s. – Quantity sufficient.

The most effective method of achieving maximum taste masking is to coat the drug particles or formulations, thereby creating a physical barrier around the bitter drug [13]. Powder layering pelletization technology is one of the best methods used to coat the drug to achieve taste masking of bitter drugs. The powder layering process is one of the most well controlled and straight forward pelletization techniques [14].

During powder layering the binding solution and finely milled powder are added simultaneously to a bed of starter seeds at a pre-determined controlled rate. In initial stages the drug particle are bound to the starter seeds of subsequently to the forming pellets with the help of a liquid bridges originated from sprayed binding liquid [15]. These liquid bridges are replaced by solid bridges derived either from a binder in the liquid medium or from any material. Successive layering of a drug and the binder solution continuous until desired pellet size are reached [16]. An important factor that needs to be considered is the particle size of the powder. Micronized particles tend to provide pellets that are smooth in appearance. If the particle size of powder is large, the amount of binder required to immobilize the particles onto the cores will be high, and consequently, pellets of low potency are produced. The morphology of the finished pellets also tends to be rough and may adversely affect the coating process and the coated product [17].

Moreover, because particles detach easily from the core they are being layered on owing to frictional forces, yield is usually low. In order to achieve the desired pellet size, successive layering of the powder and binder solution is continued [18]. In the current study, we have attempted to investigate papaya seeds for their claimed anthelmintic activity and formulated as pellets form.

MATERIAL AND METHODS:

The Papaya seeds were obtained from Gadchiroli, Maharashtra, India. The Dextrin white, Carrageenan, Chitosan, Sodium alginate and Arginine was purchased from Himedia Laboratories Pvt. Ltd. Mumbai, India. All other chemicals and reagents were used of analytical grade and were procured from authorized dealer.

Procedure for Extraction:

The seeds was cleaned and dried in shade at room temperature. The air-dried seeds of *Carica papaya* were powdered mechanically, passed through sieve # 40 and stored in air tight container separately and used for further extraction. The powdered material of Papaya

seeds (25 g) were extracted with 100 ml 70 % aqueous methanol by hot percolation method by using Soxhlet apparatus assembly at a controlled temperature. After complete extraction, filtered through muslin cloth and concentrated in rotary evaporator at 40-45°C under reduced pressure. Then the rest of the water was evaporated by evaporation on water bath. The extract was dried and used as a thick paste/powder [19].

Table 2. Formulation composition of anthelmintic herbal pellets.

Ingredients	PSP-06	PSP-07	PSP-08	PSP-09	PSP-10
Drug	25g pellets contain 10ml liquid Extract				
MCC	75	60	45	50	40
Lactose	-	-	30	30	28
β-CD	-	-	-	20	30
XG	-	20	-	-	-
GG	-	-	20	-	-
DXW	25	-	-	-	-
TCP	-	20	-	-	-
Starch	-	-	5	-	-
PVP	-	30	-	-	2
DW	q.s.	q.s.	q.s.	q.s.	q.s.

All values are expressed as %. MCC – Microcrystalline cellulose, β-CD - Cyclodextrine, XG – Xanthium gum, GG – Guar gum, TCP – Tribasic calcium Phosphate, DXW – Dextrin white, PVP – Poly vinyl pyrrodine, DW - Distilled water and q.s. – Quantity sufficient.

Physical evaluation of Papaya extracts [20,21]:

The extract of papaya in powder for was evaluated for loss on drying, Ash value and Bitter calculation as per standard prescribed procedure of Pharmacopeia specification.

Phytochemical screening of papaya extracts [22]:

The extracts of papaya in powder for was evaluated for Alkaloids, Tannins, Amino acids, Proteins, Glycosides, Carbohydrates, Flavonoids, Phenols, Saponins, Phytosterols, Triterpenoids, Phlobatannins, Quinones and Oxalates.

UV spectrophotometric study on the drug preparing the tincture [23]:

Appropriate quantity of extract was dissolved in 100 ml distilled water and the resultant tincture was studied under UV-Visible Spectrophotometer.

Anthelmintic activity of extracts:

Adult earthworms (*Pheretima posthuma)* and Cattle worms were used to evaluate anthelmintic activity *in vitro* as it is having anatomical and physiological resemblance with the intestinal round worm parasites of human beings for preliminary evaluation of anthelmintic activity [24-26].

Table 3. Qualitative chemical tests for extracts of Anthelmintic drugs.

Constituents	Aq. Extract	Aq. Methanolic extract
Flavonoids	+	+
Triterpenoids	_	_
Tannins	+	+
Amino Acid	+	+
Alkaloids	+	+
Carbohydrates	+	+
Glycosides	_	_
Saponins	+	+
Phytosterols	_	_
Phenols	+	+
Phlobatannins	_	_
Quinones	_	_
Oxalate	_	_

+ = Present and - = Absent.

Earthworms of 3-5 cm in length and 0.1 to 0.2 cm in width were collected from moist soil, washed with normal water and used for all the experimental protocol. While the cattle worms were collected from the cow dung and washed with normal water. The cattle worms of 0.5-1 cm in length were used for all experimental protocol [24-26].

Table 4. Anthelmintic activity of Papaya seed aqueous extracts on *P. posthuma*.

Group	Drug (ml/mg)	Paralysis time (min)	Death time (min)
1	Control	---	---
2	ALZ (400mg/ml)	189.33	371.50
3	AME (0.05)	200.13	442.9
4	AME (0.1)	194.2	398.50
5	AME (0.2)	165.34	368.5
6	AME (0.3)	115.27	294.25
7	CS (400mg/ml)	191.5	397.25

ALZ – Albendazole, AME – Aq. Methanolic extract and CS – Commercial sample.

Albendazole Tablet (Zim Laboratories) was used as standard anthelmintic drug during the experimental protocol. Seven groups were divided for both *P. posthuma* (n – 6) and cattle worm (n – 3). The group 1, 2, 3, 4, 5, 6, and 7 were treated with normal control; extracts dose of aq. papaya (0.3 ml/ 25 ml), aq. methanolic (0.05, 0.1, 0.2 and 0.3 ml/ 25 ml) and standard control (Albendazole 400 mg/ 25 ml). Observations were made for the time taken for paralysis of individual worm. Time for death of worms were recorded after ascertaining that worms neither moved when shaken vigorously nor when dipped in warm water.

Table 5. Anthelmintic activity of Papaya seed extracts on cattle worm.

Group	Drug (ml/mg)	Paralysis time (min)	Death time (min)
1	Control	---	---
2	ALZ (400mg/ml)	169.12	322.6
3	AME (0.05)	199.3	372.9
4	AME (0.1)	184.2	338.50
5	AME (0.2)	155.34	308.5
6	AME (0.3)	103.27	224.25
7	CS (400mg/ml)	181.9	387.3

ALZ – Albendazole, AME – Aq. Methanolic extract and CS – Commercial sample.

Pellet formulations of aq. methanolic papaya seed extract:

Papaya seeds exhibiting significant pharmacological anthelmintic activity were selected and formulated into oral pellets, prepared by coating method. For coating method, we have selected the formulations in which Dextrin white, Chitosan, Microcrystalline Cellulose, Sodium Alginate, Dibasic Calcium Phosphate, Carrageenan, and Mannitol as excipients and Arginine was used as coating material [27].

Pellets of aq. methanolic papaya seed extract prepared for external coated taste mask formulations:

For External Coated taste mask formulations primary pellets containing fixed quantity of herbal extracts were prepared by changing the concentration of extracting material (MCC, Lactose) and the polymer material. These formulations were labelled from PSP –01 to PSP –10 and composition is shown in Table 1 and Table 2. A uniform dry powder mixture (Batch size: 25 g) containing excipients was obtained by mixing in a mortar pestle for 5 min. then the Papaya seed extract was added and mixed for 10 min. A wetting solution was added as wetting agent, performed by means of a mortar pestle. To ensure uniform distribution of wetting agent during wetting phase, the material was repeatedly scrapped from the mixing mortar walls. The amount of wetting agents was different for different formulations.

Table 6. Evaluation of anthelmintic herbal pellets.

FC	BT (X±S.D.)	TD (X±S.D.)	HR	CI
PSP-01	0.71±0.016	0.77±0.102	1.077	7.15
PSP -02	0.75±0.009	0.80±0.013	1.061	5.75
PSP -03	0.69±0.015	0.75±0.019	1.094	8.62
PSP -04	0.62±0.036	0.66±0.075	1.067	6.29
PSP -05	0.77±0.087	0.81±0.039	1.061	5.75
PSP -06	0.75±0.010	0.80±0.071	1.066	6.25
PSP -07	0.67±0.014	0.72±0.033	1.070	6.62
PSP -08	0.70±0.011	0.74±0.017	1.055	5.27
PSP -09	0.72±0.021	0.75±0.059	1.038	3.71
PSP-10	0.75±0.012	0.81±0.061	1.059	6.55

Values are expresses as mean ± standard deviation (n = 3). FC – Formulation code, BD – Bulk density, TD – Tapped density, HR – Hausner ratio and CI – Carr's index.

The wet mass was then extruded at a speed of 40 rpm using a single screw extruder (Anish Pharma Equipment Pvt. Ltd.) equipped with a dome-shaped extrusion screen. The extrudates were spheronized at 550 - 950 rpm for 5 - 15 min in a spheronizer with a cross-hatched friction plate. The time for spheronization was changed for different formulations. Wet pellets were finally dried for 20 - 30 min. at 50 °C in a tray dryer or at room temperature for 2 h. The pellets were sieved using sieve no. 22 for uniform size distribution. Amongst all the formulation PSP-04 pellet preparations passed all the tests with satisfactory results and were considered for taste masking coat [27].

Coating for PSP-04:

***Coating Materials*:**

Distilled water (100 ml) was stirred at 200 rpm for 5 min, during which 2% of PVP was added in portions, and the resulting mixture was shaken gently and stirred at 200 rpm for 1 h, and then filtered. This prepared solution was used as the plasticizer for plasticizing the

base pellets during coating. The amino acids like Glycine, Alanine and Arginine was micronized in a mortar pestle and the micronized material was used as coating material for powder layering on PSP-04 base pellets [28].

Table 7. Evaluation of anthelmintic herbal pellets.

FC	AOR (°) (X±S.D.)	FBT (%)	DT (min) (X±S.D.)	AD («m)
PSP-01	26±1.01	0.74	15±0.65	872.4
PSP -02	28±0.84	0.89	13±0.71	881.7
PSP -03	29±0.92	0.93	11±0.59	830.0
PSP -04	27±0.59	0.86	8±0.29	831.7
PSP -05	27±0.39	0.79	18±0.50	671.2
PSP -06	29±0.71	0.91	21±1.03	680.5
PSP -07	25±0.68	0.64	22±0.82	859.8
PSP -08	27±0.87	0.68	21±0.42	498.9
PSP -09	26±0.65	0.62	21±0.81	542.2
PSP-10	28±0.62	0.63	20±1.02	773.5

Values are expresses as mean ± standard deviation (n = 3). FC – Formulation code, AOR – Angle of Repose, FBD – Friability, DT – Disintegration time and AD – Avg. diameter.

Coating of pellets:

Pellets (30 g) were coated using a bottom-spray fluid-bed coating technique with working model prepared in the Gurunanak College of Pharmacy, Nagpur. Prior to solution spraying, pellets were pre-heated to 30 to 45 °C. The Plasticizer solution was sprayed at a rate of 1-2 ml/min, through the upper inlet by using 50 ml syringe. After complete wetting of the pellets the micronized amino acid was sprayed through the upper inlet by using 50 ml syringe.

The same procedure was continued for 2 h to achieve uniform coated pellets. These coated pellets were removed and air dried for 30 min. Amongst the various coatings, the formulation PSP-04-G was found to be suitable for further studies as it satisfy the properties of good pellets and taste masking [28].

Characterisation of Pellets [28-30]:

In order to meet the requirements of pellet yield, size distribution, surface area, shape, surface roughness, density and friability, including the reproducibility of morphologic properties of the pellets, pellets were tested.

Table 8. Evaluation results of Coated taste masking pellet formulations.

FC	WG (%)	DT (min)	AD («m)	HSR
PSP-04-G	5	8.46±1.12	832.4	5
PSP-04-A	5	9.57±1.24	832.2	4
PSP-04-Ar	5	9.55±1.25	832.8	3

FC – Formulation code, WG – Weight gain, DT – Disintegration time, AD – Avg. diameter and HSR – Hedonic Scale Rating.

Table 9. Evaluation results of Coated taste masking pellet formulations

FC	WG (%)	DT (min)	AD («m)	HSR
PSP-04-G-I	5	8.46±1.12	832.4	5
PSP-04-G-II	7.5	9.24±0.59	834.1	5
PSP-04-G-III	10	9.40±1.25	835.8	6

FC – Formulation code, WG – Weight gain, DT – Disintegration time, AD – Avg. diameter and HSR – Hedonic Scale Rating.

Pellet yield:

The coated pellets (20 g) were sieved for 5 min on sieve shaker equipped with series of sieves of pore opening as 1400, 1000, 710, 500 and 250 µm sieves (Sieve No. 12, 16, 22, 30 and 60 respectively). The pellet yield was calculated based on the pellet fraction between 710 and 1400 µm and presented as a percentage of the total pellet weight. This size fraction was used for all further measurements.

Size analysis:

The size of pellets was determined by sieving analysis. The average diameter is calculated using the equation;

Avg. Diameter = [Σ(% R)×(MA)]/100 …….. (1)

Where, R is retained and MA is mean aperture.

Table 10. Anthelmintic activity of bitter herb pellet formulations.

Groups	Dose	Earthworms		Cattle worms	
		PT (min)	DT (min)	PT (min)	DT (min)
Control	-	-	-	-	-
Alb	16mg/ml	189.3	371.5	169.1	322.6
PSP–04-G-III	500mg	210.3	397.6	190.4	358.4
	600mg	190.5	380.1	165.2	318.2

Control – Normal saline water, PT – Paralisis time and DT – Death time.

Shape analysis:

At least 20 pellets from each batch were randomly selected for shape analysis from fraction obtained after size analysis by sieving. The pellets were mounted on a

surface of motic microscope, and the images of the pellets were captured. The area of the images and the maximum and minimum radii were calculated, and from these the various shape factors were calculated.

Flow properties:

The flow properties of prepared pellets was determined by calculating bulk density, true density, Hausner's ratio, Carr's Index and angle of repose.

Pellet Friability test:

The friability of pellets was determined by using Roche Friabilator. About 10 g of pellets (Fs) was placed in friability test apparatus together with 20 glass beads. The sample was subjected to falling shocks for 4 min at a rotational speed of 25 rpm and fines collected by sieving through 250 µm meshes. The weight difference was obtained and percentage loss was calculated.

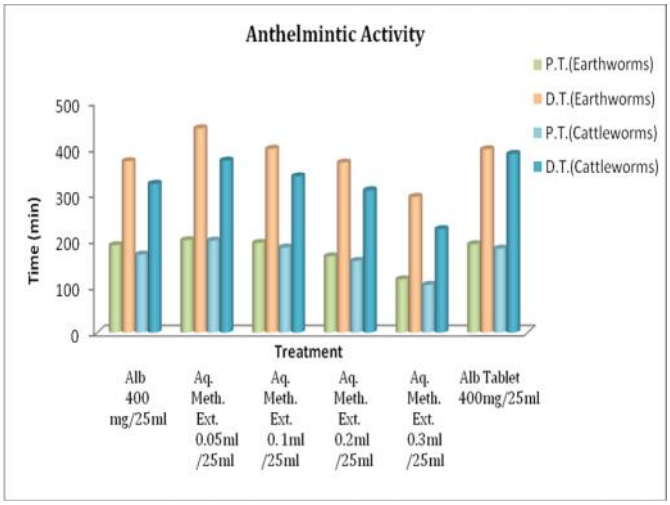

Fig 1. Anthelmintic activity of Papaya seed extracts.

Pellet Disintegration test:

The pellet disintegration in water was evaluated by atablet disintegration test apparatus. About 100 mg pellets were placed along with a plastic disc in each tube and they were inserted in the disintegration test apparatus containing 0.1N HCl maintained at 37°C ± 1°C. Disintegration test was carried out three times for each formulation, and results were expressed with the standard deviations.

Evaluation of taste masking of Papaya seed extract:

Gustatory sensation test for taste masking:

The gustatory sensation test was carried out in six healthy male volunteers. The taste masking efficiency of the used methods were analysed by gustatory sensation test where the level of taste masking was rated using a Hedonic Rating Scale for taste perception.

Taste masking test using Dissolution Method:

The pellet formulations PSP/I-03 b and PSP-04 were subjected to micro-dissolution method, by using 20 ml of pH 6.8 phosphate buffer as a dissolution medium maintained at 37±1 °C. The stirring speed was kept constant at 50 rpm. At predetermined intervals of study (1 to 5 min), 1 ml of sample was withdrawn and after every withdrawal 1ml of fresh dissolution medium was replaced. The samples were analysed either spectrophotometrically at 190-700 nm or was spotted for TLC analysis.

Thin Layer Chromatography:

The extracts were tested by thin-layer chromatography (TLC). Normal phase analytical TLC was performed on 3×5 cm silica gel (0.5 mm thickness) coated glass plates activated at 100-105 °C for 1 h. The Papaya seed extract (as reference) was applied to the chromatographic plate containing silica gel G, beside the dissolution sample taken at the end of 5 min. The plates were eluted in solvent system; Ethylacetate: Chloroform: Acetone (5: 4: 1). The eluted plates were air dried and developed using vanillin: sulphuric acid (1 g: 100ml) reagent followed by heating at 100 °C for 10 min. The compounds were deleted by the characteristic colours of the spots and R_f values.

Spectrophotometric evaluation (UV analysis):

The extracts were tested by Spectrophotometric Evaluation (UV Analysis). The dissolution sample at predetermined interval of study (1 to 5 min), after every withdrawal the samples were analysed spectrophotometrically at 190-700 nm.

***In vitro* dissolution study of pellets of papaya seed extracts:**

The ability of the enteric coated pellets of papaya seed extract PSP-04 to remain intact and to release the active ingredient in the physiological environment of intestine was assessed by conducting *in vitro* drug release studies under conditions mimicking mouth to intestine. The drug release studies were carried out using USP standard dissolution apparatus-II (basket method) at stirring speed of 50 rpm at 37±1 °C in 900 ml of dissolution medium. Initially the pH of dissolution was kept 1.2 for 2 h using 0.1M Hydrochloric acid as the average gastric emptying time was estimated at 2 h. After two hours the pH of dissolution medium was adjusted to 6.8 using 1M NaOH solution and dissolution was continued. At predetermined intervals of study, 1 ml of sample was

withdrawn at periodic intervals and it was made up to 10 ml with buffer solution. After every withdrawal 1ml of fresh dissolution medium was replaced. The samples were analysed spectrophotometrically at 276.2 nm. The dissolution experiments were conducted in triplicate and the means of the absorbance were calculated [30].

Anthelmintic screening of formulations:

For screening of anthelmintic activity, 500 mg of pellets (Containing Papaya seed extract) were crushed and to it 25 ml of distilled water was added. This mixture was added into a petridish containing 6 equal size earthworms of 3 to 5 cm in length and 0.1 to 0.2 cm in width to observe the paralysis and death time. In the study four groups were divided by taking 6 earthworms in each group. First group received (Control) normal saline water, second group received standard drug i.e. Albendazole (16 mg/ml), third and forth groups received PSP-04 of dose 500 and 600 mg pellets/ 25 ml [25,26].

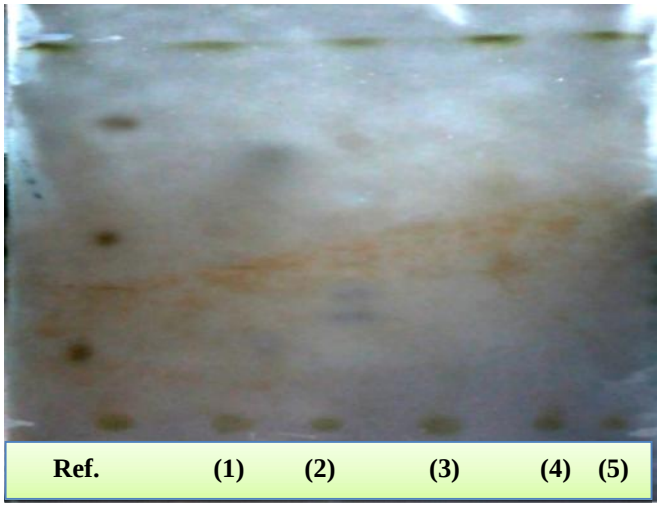

Fig 2. TLC plates of Papaya seed extract and 5 min dissolution sample of Coated pellets in Ethyl acetate : Chloroform : Acetone (5:4:1).

RESULT AND DISCUSSION:

The physical evaluation result of papaya extract showed that the loss on drying, ash values and total bitter were 9.14, 8.63 and 3.24 % respectively. The papaya extract contained Alkaloids, Tannins, amino acids, Proteins, Carbohydrates, Flavonoids, Phenols and Saponins as phytochemicals (Table 3). The Anthelmintic activity was carried out and compared with standard drug Albendazole. The result from the study is tabulated in Table 4, 5 and Fig 1. On screening of prepared extract, the anthelmintic activity was observed for aqueous methanolic extract on 0.2 ml/25ml as compared with Albendazole and the activity of papaya seed was time and dose dependent. The higher doses of aqueous methanolic extract resulted in an early onset of activity and higher number of death of earthworms occurred compared with lower doses. The aqueous methanolic extract of Papaya seed at 8 mg/ml exhibited paralysis of earthworms and cattle worms on 179 and 155.34 min and showed paralysis of on 155.34 min after exposure and death of earthworms and cattle and death was on 345.5 and 308.5 min of exposure respectively. All the earthworms exposed to Albendazole solution were found to be paralyzed at 189.33 min and their death at 371.5 min while cattle worms exposed to Albendazole solution were found to be paralyzed at 169.12 min and their death at 322.6 min, which was less than the papaya extract activity. Whereas, none of the earthworms was found dead or paralyzed in distilled water. The solution of marketed tablet of Albendazole also exhibited significant activity.

Table 1 and 2 presented formulation design of pellet formulations. From the above evaluation it was observed that pellet formulations PSP-04 containing dextrin white showed faster disintegration and better sphericity. Hence PSP-04 was selected for further experiment. The optimised formulation i.e. PSP-04 was further coated with amino acids. Amongst the various ratio, the formulation PSP-04-G was found to be suitable for further studies as it satisfy the properties of good pellets Taste masked formulation. Almost all pellet formulations exhibited good physichochemical properties as evident from Table 6 and 7. PSP-04-G formulation was considered constant and the coating level of glycine was varied to prepare formulations PSP-04-G-I to PSP-04-G-III (Table 8).

The taste perception studies in order to evaluate the efficiency of Coated taste masking formulations of pellet of papaya seed extract was carried out using Hedonic scale rating. By selecting the appropriate excipients, it was possible to modify the taste of papaya pellet. Similarly in the coated taste masking pellet formulations PSP-04-G-III indicates good taste masking effect (Table 9). Chromatographic evaluation of Extracts and formulations was done using Thin Layer Chromatography (TLC). The compounds were detected by the characteristic colours of the spots and R_f values. When TLC study were conducted by selecting Ethyl acetate: Chloroform: Acetone (5:4:1) as mobile phase. Results obtained are depicted in Fig 2. It shows maximum R_f values of various colours. When the

sample run of 1-5 min micro-dissolution of coated taste mask pellet formulation does not show the spots.

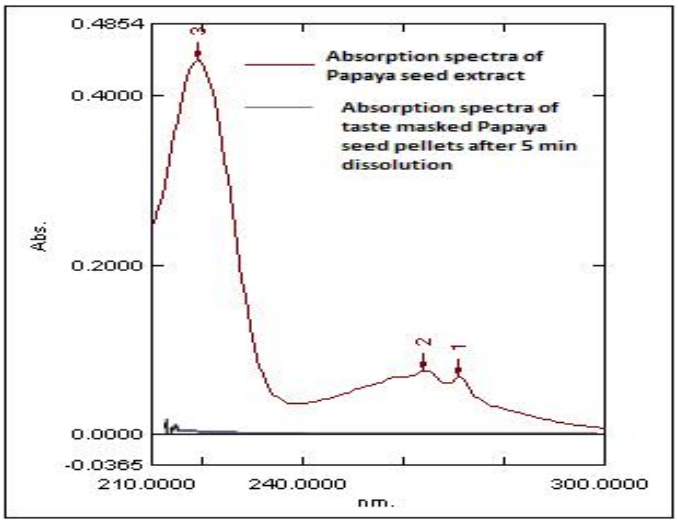

Fig 3. Absorption spectra of Papaya seed extract and PSP-04-G-III after 5 min dissolution.

The chromatographic evaluation shows that the formulations of Coated pellets are taste masked since no bitter was released within 5 min period.

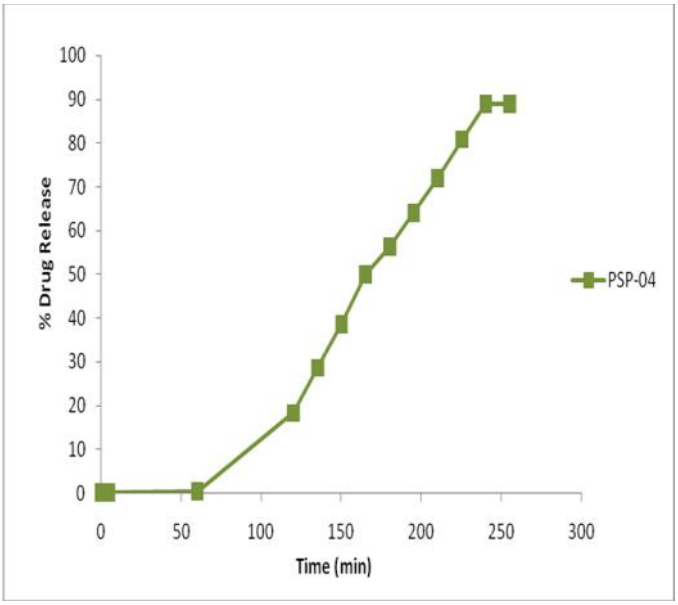

Fig 4. The % release of Papaya seed extract pellets.

The pellets were subjected to micro-dissolution test and samples in time interval 1 to 5 min were analysed spectrophotometrically for release of bitters from the coated taste mask formulation. The absorption spectra of coated taste masking pellet formulation PSP-04-G-III does not show any absorbance it may be concluded that the bitter taste would be masked *in vivo*.

The *in vitro* dissolution study of Papaya seed pellets was carried out using PSP-04-G-III Pellets formulations. In ethanol Papaya seed extract was showed the absorption peak at 276.2 nm (Fig 3). The formulated taste mask pellets of Papaya seed extract were subjected to *in vitro* drug release studies to study the release of the active constituents of papaya seed extract in the physiological environment of stomach and intestine i.e. at pH 1.2 and pH 6.8 phosphate buffer. The results of *in vitro* drug release study of PSP-04-G-III were shown in Fig 4. The percentage of papaya seed extract released for first 2 h from the above formulations in pH 1.2 was negligible due to pH sensitive Eudragit in non coated pellets and microbial triggered polymer in coated pellets. In the pH 6.8 drugs started to release from both the batches of pellet formulations.

The total amount of drug release from PSP-04-G-III was found to be 88.99 %. Anthelmintic activity was carried out using Earthworms and compared with standard Albendazole solution, results of the study parameters are summarized in Table 10. Anthelmintic activity of formulations and comparison with standard (Albendazole) indicated that, prepared formulations exhibited comparable and significant activity (Fig 5).

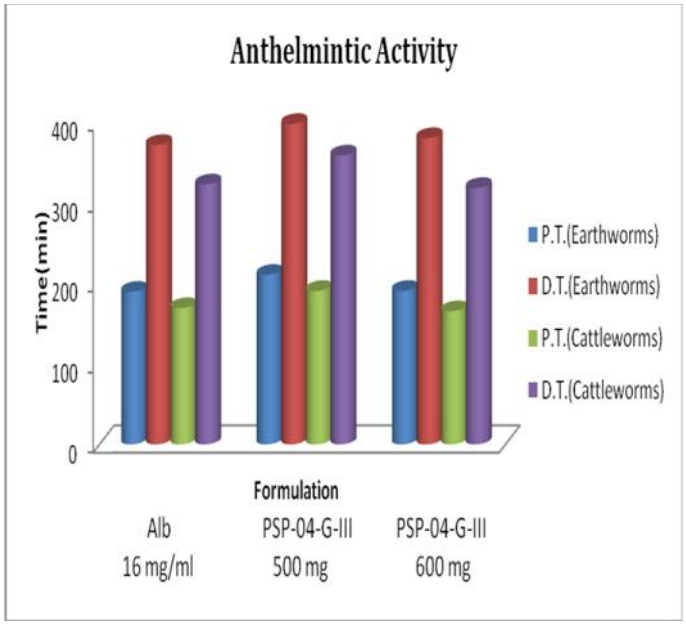

Fig 5. Anthelmintic activity of bitter herb pellet formulations.

CONCLUSION:

In the present study concluded that the Papaya seed pellets were proposed as alternatives to tablets breaking, as they offer more flexibility for dose adaptation to a child's body weight. They were produced by taste masking method via extrusion-spheronization. Based on dissolution and the chromatographic data, the taste masking efficiency of pellets was found to be

satisfactory. The papaya seed extract pellet exhibited significant anthelmintic activity with good commercial properties. Thus papaya pellet could be use for safe and successful management of worm infection in child.

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