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Design, formulation and evaluation of a colon specific drug delivery system for a model anthelminthic drug-Ivermectin

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ABSTRACT

The objective of the present study is to develop colon targeted drug delivery system for Ivermectin using guar gum as a carrier in the treatment of Helminthiasis. Matrix tablets containing various proportions of guar gum were prepared by wet granulation technique using starch paste as a binder. The idea was that the enteric coating would prevent drug release and absorption in the upper gastrointestinal tract. Use of organic acids as additional excipients might further delay drug dissolution and absorption. All the formulations were evaluated for hardness, drug content uniformity and were subjected to in vitro drug release studies. The amount of Ivermectin released from the matrix tablets at different time intervals was estimated by a UV Spectroscopy method. Colon targeted matrix tablet of Ivermectin containing 45% Guar gum released no Ivermectin in the physiological environment of stomach (0.1N HCL) and small intestine (phosphate buffer 7.4pH). When the dissolution study was continued in simulated colonic fluids (Phosphate buffer 6.8 pH) the matrix tablets released 94% and in simulated colonic fluids (rat caecal content medium) the matrix tablets released another 98% of Ivermectin after degradation into 2-3 pieces at the end of the 24 h study. The result of the studies showed that colon targeted matrix tablet containing 45% of guar gum was most likely to provide targeting of ivermectin for local action in the colon. The colon targeted matrix tablet of ivermectin showed no change either in physical appearance, drug content or in dissolution pattern after storage at $30^0 \pm 2^0$C / 65%±5% RH for 2 month.

Keywords: Colon targeted matrix tablet, Ivermectin, Guar gum, Rat caecal content.

INTRODUCTION

Helminthiasis is a disease in which a part of the body is infested with worm such as pinworm, hookworm, roundworm or tapeworm. Typically, the worms reside in the gastrointestinal tract but may also burrow into the liver and other organs.

Types of Infection

- Schistosomiasis
- Ascariasis
- Trichuriasis
- Hookworm
- Onchocerciasis
- Filariasis.[1]

Anthelmintics are drugs that either kill (vermicide) or expel (vermifuge) infesting Helminths. Helminthiasis is prevalent globally (1/3 of world population harbours then), but it is more common in developing countries like India, Asia, Mexico, Central and South America with poorer personal and environmental hygiene especially in areas with water that is contaminated with freshwater snails, which may carry the parasite. In human body, GIT is the abode of many helminths. They harm the host by depriving him of food, causing blood loss, injury to organs, intestinal or lympathic obstruction and by secreting toxins. Helminthiasis is rarely fatal, but is a major cause of ill health worldwide.

Helminthiasis is a parasitic infection. The choice of drug for each worm infestation is based not only on efficacy, but also on lack of side effects/toxicity, ease of administration (preferably single dose) and Low cost. Development of resistance has not been a problem in the clinical use of Anthelmintics.[2]

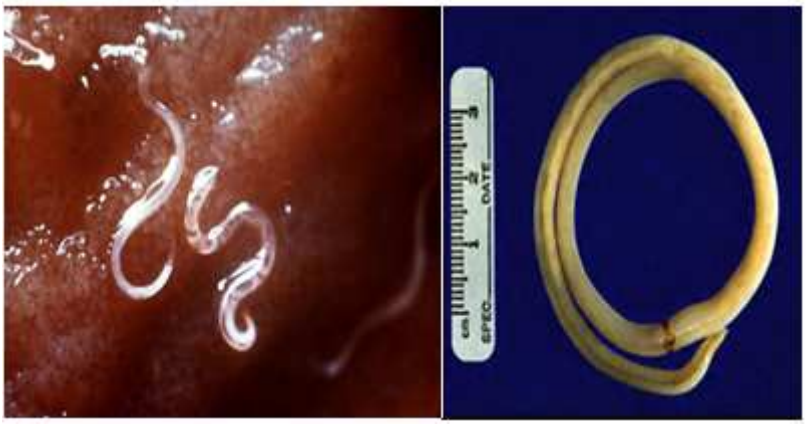

Figure1: Hook Worm

The current choice of drugs for worm infestations common in Indian subcontinent is given below Mebendazole, Albendazole , Pyrantel , Thiabendazole , Diethylcarbamazine, Niridazole, Praziquantel, Ivermectin which are used for Round worm (Ascaris Lambricoides), Hook worm (Ancylostoma duodenale), Thread worm (Enterobius vermiculasis), whip worm, Filaria, Guinea worm, Tape worm.

The most preferred choice of drugs for Helminthiasis is Ivermectin this drug should be delivered to colon for its effective action against helminths. The administration of this drug in conventional tablet dosage form provides minimal amount of Ivermectin for local action in the colon, still resulting in the relief of helminths, but with unwanted systemic side effects. The oral route is considered to be most convenient for administration of drugs to patients. Oral administration of conventional dosage forms normally dissolves in stomach fluid and gets absorbed from these regions of the gastrointestinal tract. It is a serious drawback in

conditions where localized delivery of the drugs in the colon is required or in conditions where a drug needs to be protected from the hostile environment of upper GIT. Dosage forms that deliver drugs into the colon rather than upper GIT proffers number of advantages.

The colon is rich in lymphoid tissue, uptake of antigens into the mast cells of the colonic mucosa produces rapid local production of antibodies and this helps in efficient vaccine delivery. The colon is attracting interest as a site where poorly absorbed drug molecule may have an improved bioavailability. This region of the colon is recognized as having a somewhat less hostile environment with less diversity and intensity of activity than the stomach and small intestine. Additionally, the colon has a longer retention time and appears highly responsive to agents that enhance the absorption of poorly absorbed drugs. Apart from retarding or targeting dosage forms, a reliable colonic drug delivery could also be an important starting position for the colonic absorption of per orally applied, undigested, unchanged and fully active peptide drugs [2].

Advantage of colon targeted drug delivery

- The dose of the drug can be reduced to achieve the desire effects.
- Avoidance hepatic first pass metabolism.
- Enhancement of the absorption of large molecule such as protein & peptide.
- Delivering the drug to its target site can reduces toxicity and harmful systemic effects of a drug.
- Toxicity can be reduced by administrating the drug in a non-toxic form (prodrug) that gets activated in the target site [3].

So in order to achieve above advantages, in the present study Ivermectin matrix tablet were been used to target colon for the treatment of Helminthiasis.

EXPERIMENTAL SECTION

➢ Preparation of reagents & solutions

1. Preparation of 0.1 N HCl:

0.1N HCl was prepared by diluting 8.5 ml of concentrated hydrochloric acid to 1000 ml with distilled water[4].

2. Preparation of pH-6.8 phosphate buffer:

28.80 g of disodium hydrogen phosphate & 11.45g of potassium hydrogen phosphate were dissolved in water & volume was made up to 1000ml[4].

3. Preparation of pH-7.4 phosphate buffer:

2.38 g of disodium hydrogen phosphate, 0.19 g of potassium dihydrogen phosphate & 8.0 g of sodium chloride were dissolved in water & volume was made up to 1000 ml. Adjust the pH if required[4].

4. Preparation of pH-6.8 phosphate buffer with 4% w/v rat caecal contents:

Male Wistar rats weighing 105-115 gm and maintained on a normal diet were used for the study. Thirty minutes before the commencement of drug release studies, four rats were killed by spinal traction. The abdomen were opened, the caecal were traced, ligated at both ends, dissected and immediately transferred into pH-6.8 phosphate buffer, previously bubbled with carbon dioxide gas. The caecal bags were opened; their contents were individually weighed,

pooled and then suspended in pH-6.8 phosphate buffer to give 4 %w/v dilution. As the cecum is naturally anaerobic, all these operations were carried out under carbon dioxide gas [5], [6]. The care of the rats was in accordance with institutional guidelines.

5. Preparation of Coating solution:

1. Eudragit L -100 10% w/v was prepared using acetone solution.
2. PEG 4000 1% w/v was prepared using acetone solution.

➢ **Preparation of calibration curve of Ivermectin**

1. Preparation of calibration curve in 0.1 N HCl:

The stock solution (100 µg/ml) was diluted in 0.1 N HCl. Serial dilutions were carried out so as to get different concentration 5, 10, 15, 20, 25 µg/ml. The absorbance was measured at 245 nm using U.V spectrophotometer against blank. The procedure was performed in triplicate to validate the calibration curve.

2. Preparation of calibration curve in phosphate buffer 7.4 pH:

The stock solution (100 µg/ml) was diluted in phosphate buffer 7.4 pH. Serial dilutions were carried out so as to get different concentration 5, 10, 15, 20, 25 µg/ml. The absorbance was measured at 245 nm using U.V spectrophotometer against blank. The procedure was performed in triplicate to validate the calibration curve.

3. Preparation of calibration curve in 6.8 pH:

The stock solution (100 µg/ml) was diluted in phosphate buffer 6.8 pH. Serial dilutions were carried out so as to get different concentration 5, 10, 15, 20, 25 µg/ml. The absorbance was measured at 245 nm using U.V spectrophotometer against blank. The procedure was performed in triplicate to validate the calibration curve.

4. Preparation of calibration curve in 6.8 pH with rat caecal content:

The stock solution (100 µg/ml) further diluted in phosphate buffer 6.8 pH with rat caecal content. Serial dilutions were carried out so as to get different concentration 5, 10, 15, 20, 25 µg/ml. The absorbance was measured at 245 nm using U.V spectrophotometer against blank. The procedure was performed in triplicate to validate the calibration curve [7].

Formulation of colon targeted matrix tablet of Ivermectin

Matrix tablet of Ivermectin were prepared by the wet granulation technique using 10 % starch paste. HPMC was used as diluent and the mixture of talc & magnesium stearate at 2:1 ratio was used as lubricant. The composition of different matrix formulation used in the study containing 10 mg of Ivermectin is given in table. In the all formulation guar gum was sieved (sieve no. 60) separately and mixed with Ivermectin (sieve no. 100) and HPMC (sieve no. 60). The powder were blended and granulated with 10% starch paste. The wet mass was obtained which as then passed through a mess (1190 µm). And the wet granules were dried at 50^0C for 2 hours. The dried granules were passed through a mess (1000 µm or sieve no.16) and were lubricated with a mixture of talc & magnesium stearate (2:1). The lubricated granules were compressed at compression force 4000-5000 kg using 8mm flat punch on tabletting machine. The tablets were coated with a 10%w/v solution of Eudragit L-100, using a pan coating equipment. PEG-4000 (1%w/v) was used as a plasticizer. The percent weight increase of each group of formulation of tablets after coating varied between 2.0± 0.005% w/w [8].

Formulation	Ivermectin	Guar gum		HPMC E50LV		Starch	Citric Acid	Mg-Stearate	Talc	Total Wt.
Code	(mg)	(%)	(mg)	(%)	(mg)	(mg)	(mg)	(mg)	(mg)	(mg)
IF1	10	7.5	18.75	62.5	156.25	25	25	5	10	250
IF2	10	15	37.Z5	55	137.5	25	25	5	10	250
IF3	10	22.5	56.25	47.5	118.75	25	25	5	10	250
IF4	10	30	75	40	100	25	25	5	10	250
IF5	10	37.5	93.75	32.5	81.25	25	25	5	10	250
IF6	10	45	112.5	25	62.5	25	25	5	10	250
IF7	10	52.5	131.25	17.5	43.75	25	25	5	10	250
IF8	10	60	150	10	25	25	25	5	10	250

Table 1: Formulation of colon targeted matrix tablet

Evaluation of colon targeted matrix tablets of Ivermectin

Pre-formulation studies

Drug- excipient compatibility studies

This can be carrying out by Fourier Transform-Infrared absorption scanning spectroscopy (FT-IR) studies.Infra red spectra of pure drug & mixture of formulation were recorded by dispersion of drug & mixture of formulation in suitable solvent (neat) using Fourier Transform Infrared Spectrophotometer. A base line correction was made using dried potassium bromide and then the spectra of the dried mixture of drug, formulation mixture and potassium bromide were recorded on FTIR at IISc, Bangalore.

Physicochemical Parameters

1. Thickness of Tablets:

The thickness of six tablets was measured using vernier calipers. The extent to which the thickness of each tablet deviated from ± 5% of the standard value was determined [9], [10], [11] [12],[13].

2. **Hardness and Friability of Tablets**:

Hardness of the Tablet was determined by Monsanto Hardness Tester. Six tablets from each batch were selected and evaluated, and the average value with standard deviation was recorded [9-13].

Friability of Tablets was performed in a Roche Friabilator. Ten tablets were weighed together and then placed in the chamber. The friabilator was operated for 100 revolutions and the tablets were subjected to the combined effects of abrasion and shock because the plastic chamber carrying the tablets drops them at a distance of six inches with every revolution. The tablets are then dusted and re-weighed [9-13].

3. Weight Variation and Uniformity of Drug content.

Weight variation test: Uniformity of weight test as described in the IP was followed. Twenty tablets were selected at random and average weight was determined. Then individual tablets were weighed and the individual weight was compared with the average weight. The percentage deviation was calculated and checked for weight variation. Using this procedure weight variation range of all batches of formulations were determined and recorded[9-13].

Uniformity of drug content: The matrix tablets of Ivermectin were tested for their drug content. Weigh and powder 20 tablets. Quantity of the powder equivalent to 15 mg of Ivermectin was weighed & dissolve in 20 ml of methanol, shake well and add sufficient methanol to produced 100 ml. Mix well & filter. Diluted 10 ml of the above solution with

methanol & further diluted 10 ml of this solution to 100 ml with methanol. Measure the absorbance of resulting solution as per the method described above[9-13].

4. *In-vitro* dissolution Studies:

In-vitro dissolution study was performed by using USP Type II Apparatus (Basket type) [Electrolab (ETC-11L) Tablet Dissolution Tester] at 100 rpm for 2 h in 0.1 N HCl (900 ml).Then the dissolution medium was replaced with pH 7.4 phosphate buffer (900 ml) and tested for 3 h as the average transit time of small intestine is 3 h. After 5 h, the dissolution medium was replaced with pH 6.8 phosphate buffer and tested for next 19 h. At the end of the time period 10 ml of the sample were taken and analyzed for Ivermectin content as described previously. A 10 ml fresh and filtered dissolution medium (buffers) was added to make the volume after each sample withdrawal[9-13].

5. *In-vitro* dissolution Studies in the presence of 4% w/v rat caecal content:

To assess the susceptibility of the guar gum to undergo degradation in the presence of colonic bacteria was done by continuing the drug release studies in the presence of rat caecal content medium because of the similarity of the micro flora of the rat caecal to that of the human colon. The drug release studies were carried out in USP dissolution test apparatus (apparatus 1, 100 rpm, 37°C) with slight modification. A beaker (capacity 150 ml) containing 100 ml of dissolution medium was immersed in the water contained in the 1000 ml vessel, which in turn, was the water bath of the apparatus. The swollen formulations after completing the dissolution study in 0.1 M HCl (2 h) and pH-7.4 phosphate buffer (3 h) were placed in the baskets of the apparatus and immersed in the dissolution medium containing rat caecal content medium. The drug release studies were carried out up to 24 h and 1 ml samples were withdrawn at specified time intervals without a pre- filter and replaced with 1 ml of fresh phosphate buffer. 1 ml of methanol was added in sample and was analyzed for Ivermectin content as per above described method [9-13].

Stability studies of colon targeted matrix tablet of Ivermectin

Stability Studies

Stability of a drug has been defined as the ability of a particular formulation in a specific container, to remain within its physical, chemical, therapeutic and toxicological specifications.

The purpose of stability study is to provide evidence on the quality of a drug substance or drug product which varies with time under the influence of a variety of environmental factors such as temperature, humidity and light. Recommended storage conditions, re-test periods and shelf-lives are to be established.

The International Conference of Harmonization (ICH) Guidelines titled, “stability testing of New Drug substance and products” (QIA) describes the stability test requirements for drug registration application in the European Union, Japan and the United States of America. ICH specifies the length of study and storage conditions $30^0C \pm 2^0C$ / 60% ± 5% RH for 2 months.

RESULTS

Drug-excipient compatibility studies (FT-IR study)

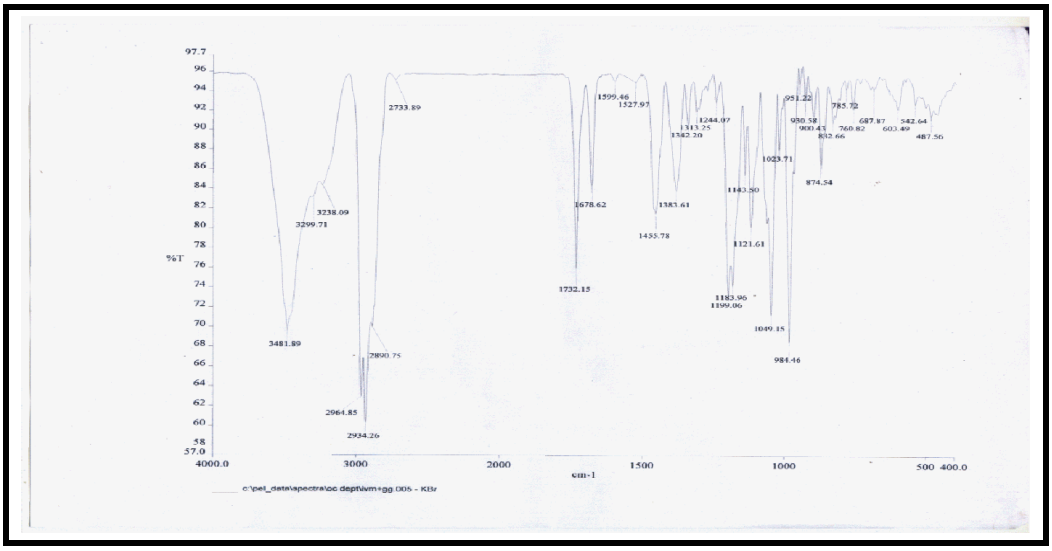

Figure 2: FT-IR spectrum of Ivermectin and Guar Gum

Preparation of calibration curve of Ivermectin:

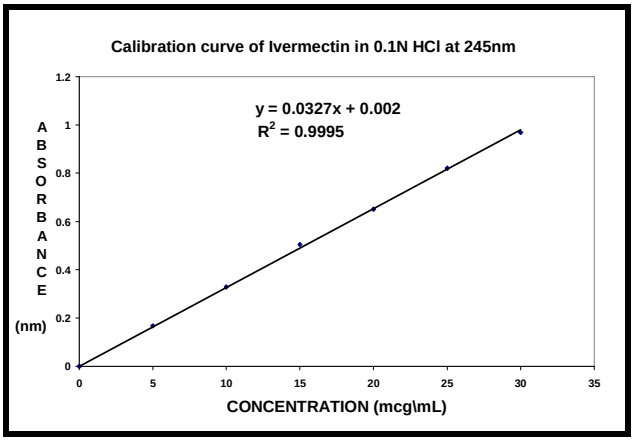

Figure 3: Standard Plot of Ivermectin in 0.1 N HCl at 245nm

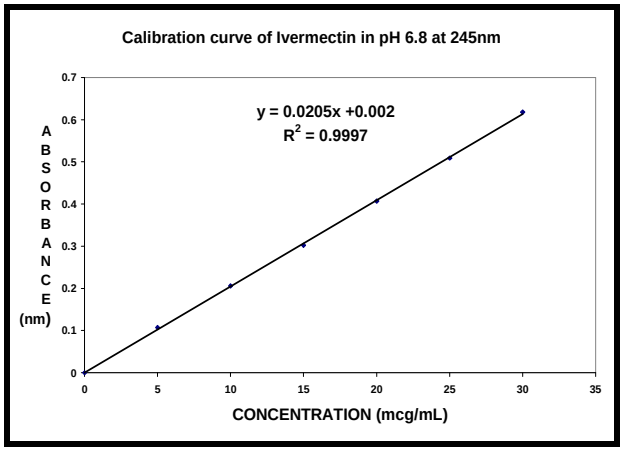

Figure 4: Standard Plot of Ivermectin in phosphate buffer pH 6.8 at245nm.

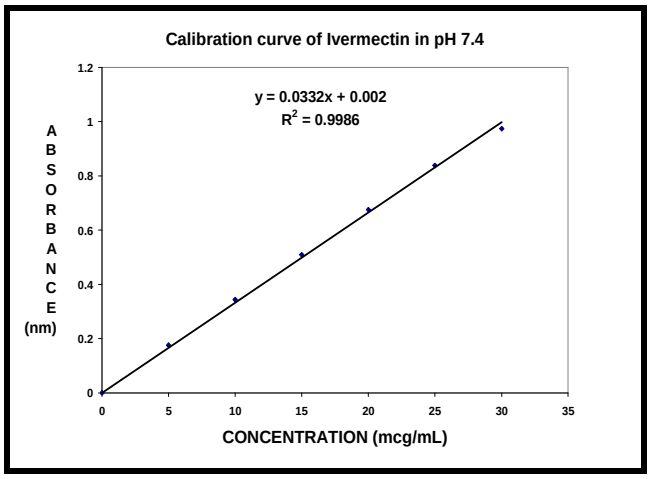

Figure 5: Standard Plot of Ivermectin in phosphate buffer pH 7.4.

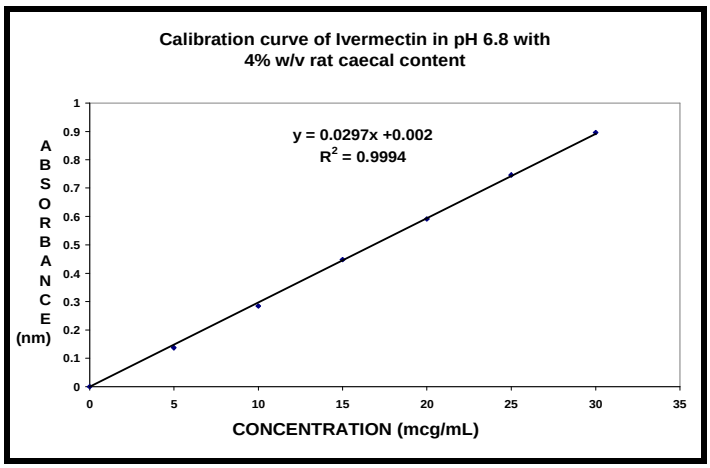

Figure 6: Calibration curve of Ivermectin in phosphate buffer pH 6.8 with 4 % w/v rat caecal content.

Physiochemical Parameters:

Thickness of colon targeted matrix tablet of Ivermectin

Table 3: Result of evaluation of thickness of colon targeted matrix tablet of Ivermectin

Formulation code	Thickness in mm ± SD
IF1	5.50 ± 0.28
IF2	5.50 ± 0.11
IF3	5.50 ± 0.07
IF4	5.25 ± 0.16
IF5	5.25 ± 0.14
IF6	5.50 ± 0.10
IF7	5.50 ± 0.01
IF8	5.50 ± 0.05

*** All values are the mean ±SD, n=3*

Hardness & Friability of tablets

Table 4: Result of evaluation of hardness of colon targeted matrix tablet of Ivermectin

Formulation code	Hardness (kg/cm^2) (±S.D)	Average hardness (kg/cm^2)
IF1	5.9±0.115	5.9±.015
IF2	6.5±0.288	
IF3	5.7±0.172	
IF4	5.9±0.152	
IF5	6.8±0.155	
IF6	6.2±0.115	
IF7	5.8±0.110	
IF8	5.8±0.115	

** All values are the mean ±SD, n=3*

Table 5: Result of evaluation Friability

Formulation code	Weight of 10 tablet before test	Weight of 10 tablet after test	% friability (±S.D)	Average
IF1	2.5 g	2.495 g	0.1 ± 0.01	0.145%
IF2	2.5 g	2.394g	0.12 ± 0.04	
IF3	2.5 g	2.494 g	0.12 ± 0.02	
IF4	2.5 g	2.294 g	0.12 ± 0.08	
IF5	2.5 g	2.493 g	0.1 ± 0.01	
IF6	2.5 g	2.396g	0.08 ± 0.03	
IF7	2.5 g	2.497g	0.12 ± 0.04	
IF8	2.5 g	2.492 g	0.04 ± 0.01	

Table 6: Result of evaluation for weight variation & drug contents of colon targeted matrix tablet formulation of Ivermectin

Formulation code	Average weight of one tablet ± SD	% drug content w/w ± SD
IF_1	250.2 ± 0.177	98.85 ± 0.0664
IF_2	250.5 ± 0.101	99.51 ± 0.0721
IF_3	255.3 ± 0.125	97.60 ± 0.0321
IF_4	247.4 ± 0.21	98.14 ± 0.0264
IF_5	255.8 ± 0.57	98.42 ± 0.0529
IF_6	252.6 ± 0.59	98.79 ± 0.0503
IF_7	250.6 ± 0.142	99.30 ± 0.0251
IF_8	251.4 ± 0.568	100.28 ± 0.085

In-vitro dissolution studies:

The ability of guar gum matrix tablet of Ivermectrin to remain intact in the physiological environment of stomach and small intestine was assessed by conducting drug release studies under condition mimicking mouth to colon transit. *In vitro* dissolution studies were performed as per the procedure described in methodology section.

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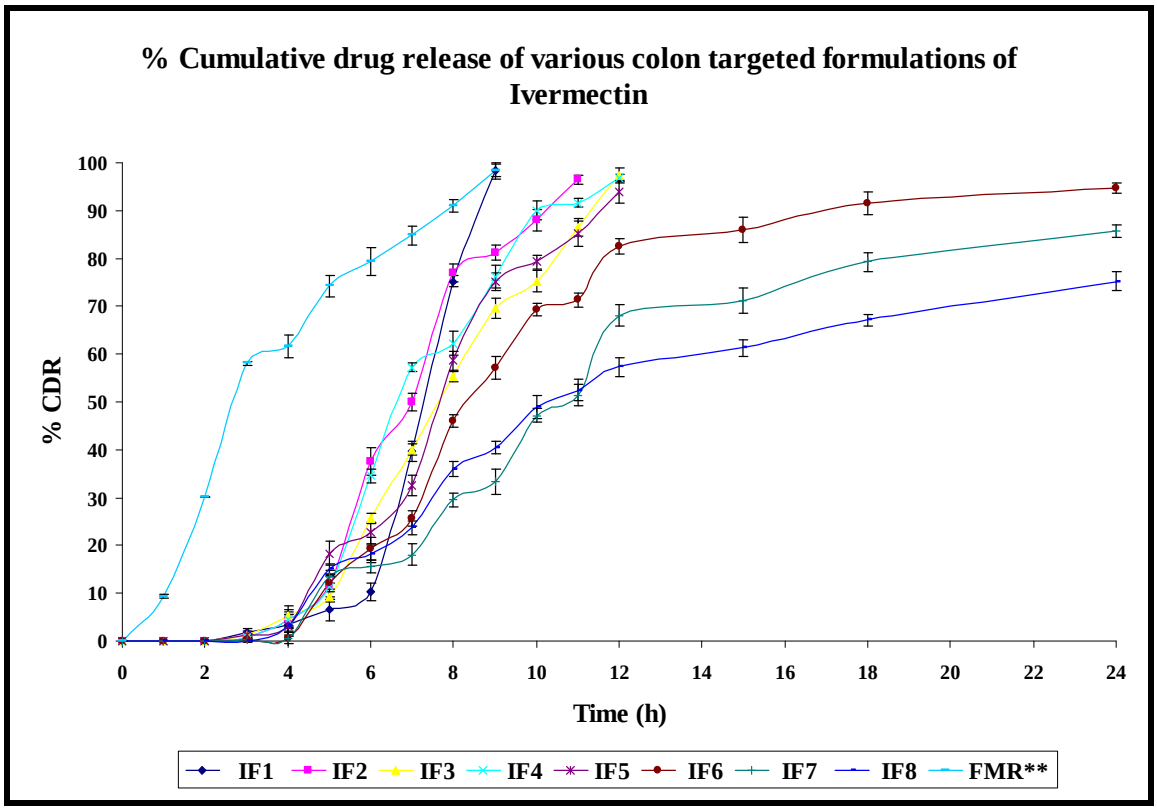

Figure 7: Cumulative % of Ivermectin release from colon targeted matrix tablet
(F_{MR}^{**} indicates the conventional marketed product)

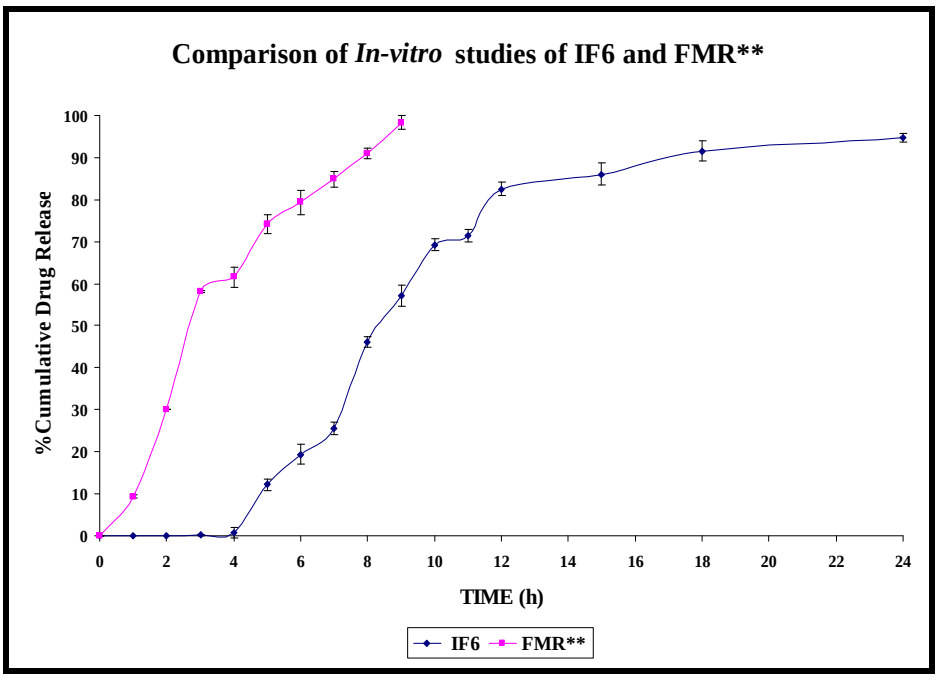

Figure 8: Comparison of *in-vitro* studies of IF_6 & F_{MR}^{**}

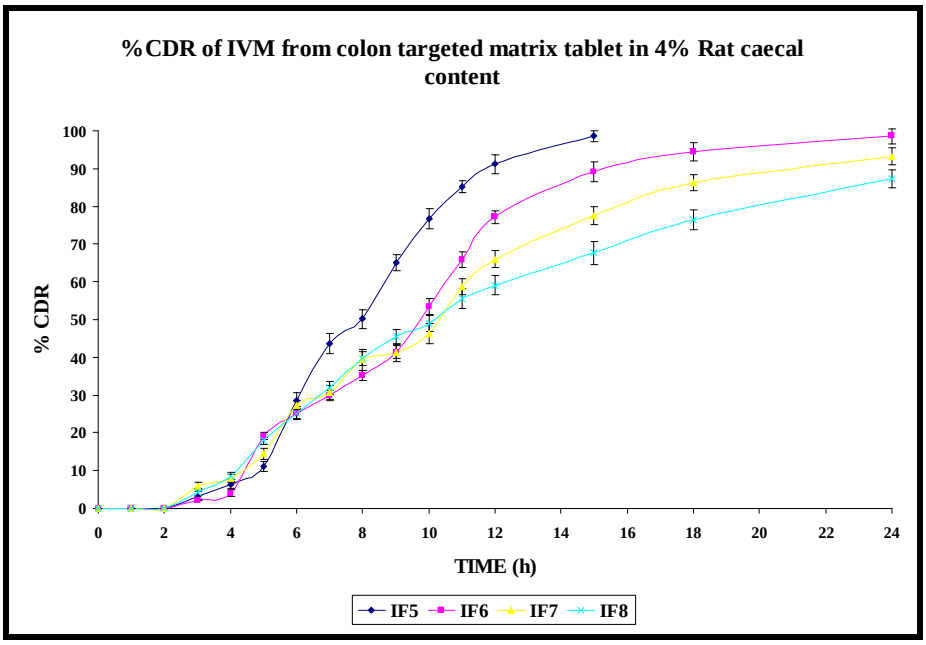

Figure 9: Cumulative percentage of Ivermectrin release from colon targeted matrix tablet in the presence of 4 % w/v rat caecal content.

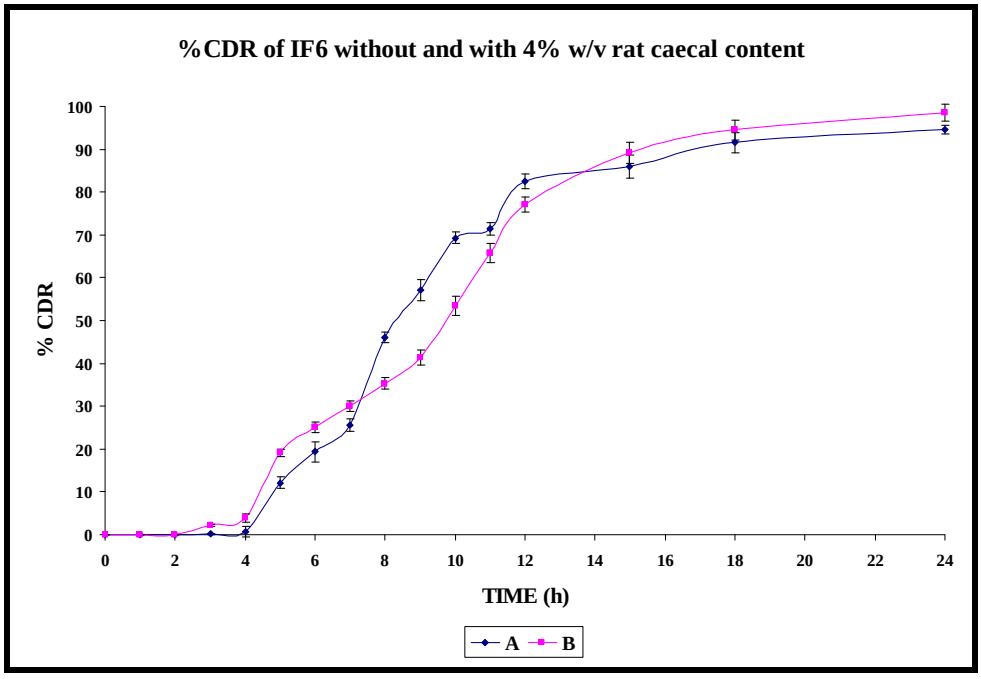

Figure 10: Cumulative percentage of drug release from IF_6 with & without 4 % w/v rat caecal content.
A= without rat caecal content, B= with rat caecal content

Stability studies of colon targeted matrix tablet of Ivermectin

Stability studies for all formulations were carried out as per the procedure in methodology section.

Table 7: Result of Evaluation for Hardness & Friability in Stability Studies of colon targeted matrix tablet at 30± 2°C / 65±5 % RH for 2 months.

		Physical Appearance Parameters	
Formulation code	**Sampling interval**	**Hardness(kg/cm^2)(±S.D)**	**Friability (%) (±S.D)**
IF_6	**Initial**	**5.9 ±0.115**	**0.07 ± 0.01**
	15 days	**5.7 ±0.112**	**0.09 ± 0.12**
	30 days	**5.2±0.125**	**0.093 ± 0.21**
	60 day	**5.2 ±0.278**	**0.091 ± 0.14**

Table 8: Result of % drug content & morphology of colon targeted matrix table after the stability studies at 30± 2°C / 65±5 % RH for 2 months

Formulation code	Sampling interval	Drug content %	Morphology (appearance)
IF_6	**Initial**	**98.49**	**----**
	1 month	**98.46**	**----**
	2 month	**98.42**	**+**

---- indicates no change in morphology , + indicates mild change in morphology (color intensity)

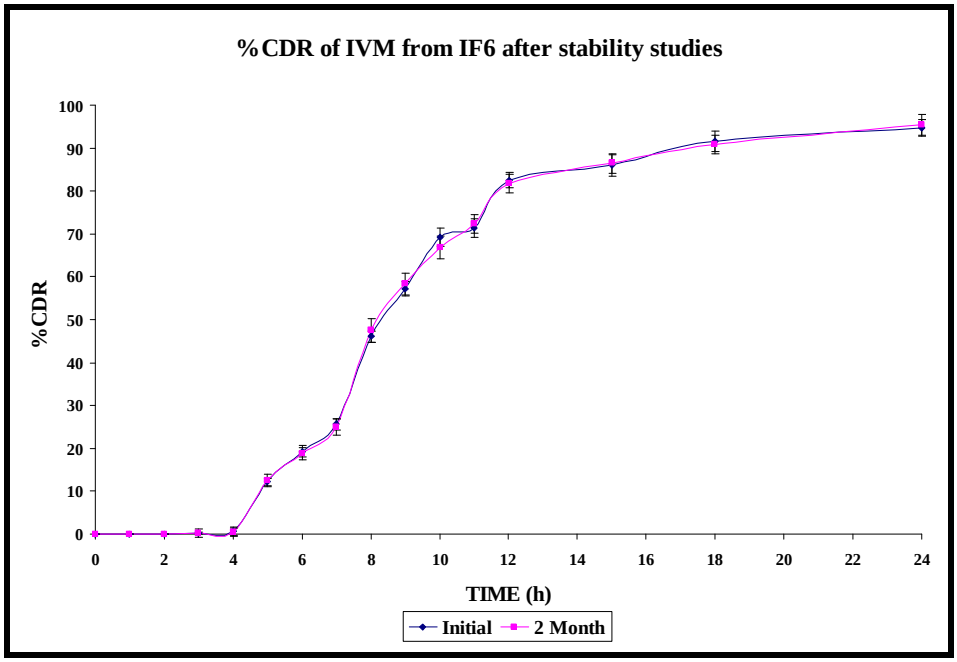

Figure-11: Percentage of Ivermectin release from IF_6 after stability studies

DISCUSSION

In the investigation, various formulations of colon targeted matrix tablet of Ivermectin were prepared by wet granulation technique using various proportion of guar gum as carrier and coated with Eudragit L-100 to target the model drug to the region of colon. In order to select the best formulation, various parameters were checked and subjected to *in vitro* dissolution studies, and their release profile was observed and compared with other formulation. Evaluation of physicochemical parameters such as appearance, bulk density, % compressibility, weight variation, friability, drug content and *in-vitro* dissolution studies were performed. All the above tests were described in Methodology. Stability studies were performed for a two month as per ICH guidelines and parameters like physical appearance, drug content uniformity, and *in-vitro* dissolution studies of the formulations were assessed.

Development of drug delivery system:
Matrix tablet of Ivermectin were prepared by the wet granulation technique using 10 % starch paste. HPMC was used as diluent and the mixture of talc & magnesium stearate at 2:1 ratio was used as lubricant. The composition of different matrix formulation used in the study containing 10 mg of Ivermectrin is given in table 1. In the present study, guar gum was incorporate at various percentages to retard the drug release in the environment of stomach & small intestine and further coating was done with 10% Eudragit-L 100. The granules were prepared by the method described in the methodology section. The lubricated granules were compressed at compression force 4000-5000 kg using 8mm flat punch on tabletting machine and then coated using the Eudragit^{TM} L-100 solution containing PEG 4000 as plasticizer.

Drug-excipient compatibility studies:
The pure drug and the formulation were subjected to FT-IR studies. This study was carried out to establish that the therapeutically active drug has not undergone any changes. After spectral comparison it was confirmed that no incompatibility reactions takes place between drug and excipients.

Thickness, Hardness and Friability of Tablets:
Thickness of all the formulations was the acceptable range of 5 mm to 5.5 mm. The average hardness of all the tablet formulations lies in the range of 5.9±.0147 kg/cm^2 the average friability of all the formulations lies around 0.145%.

Weight variation test: Average weight of the tablet was 250 mg with weight variation (250mg±5%) (245 to 255mg). Thus all the formulations were found to be complying with the standards given in IP.

Uniformity of drug content:
Uniformity of weight test for all formulations was carried out using the procedure described in methodology section and results were shown in Table 6. Good and uniform drug content (>98) was observed within the batches of different tablet formulation.

***In-vitro* dissolution studies:**
All the colon targeted matrix tablet formulations of ivermectin were evaluated for *in vitro* dissolution studies as per the procedure described in methodology section. The highest *in-vitro* dissolution profile at the end of 24 h was shown by IF_6 containing 45 % of guar gum (94.69%) followed by IF_7 containing 52.5 % of guar gum (85.76%), IF_8 containing 60 % of guar gum (75.21%). The other formulation like, IF_4 containing 30 % guar gum (96.89%), IF_3 containing 22.5 % of guar gum (97.41%), IF_2 containing 15 % of guar gum (96.45%), IF_1 containing 7.5% of guar gum (98.41%) were failed to target the Ivermectin in the colon & these formulation releases the majority of drug within 10 h of study, it may be due to the less proportion of guar gum to retard the drug release.

The *in-vitro* dissolution study of conventional marketed product was found to be F_{MR} 98.29% within 9 h, from this data it was found to be that the conventional marketed product was also failed to retard the drug release in 24 h of study period. From the *in-vitro* dissolution studies it can be discussed that the colon targeted matrix tablet containing 45% guar gum was the best formulation to target the Ivermectin to the colon in the treatment of Helminthiasis. From the *in-vitro* dissolution studies in the presence of rat caecal content it was found to be that the drug release increased in the presence of 4 % w/v rat caecal content and the colon targeted matrix tablet containing 45% guar gum released 98.62% of Ivermectin. It may be due to the

presence of colonic bacteria which act on the guar gum & digest it. Therefore released maximum quantity of Ivermectin in colon & retard the drug release in the environment of stomach & small intestine.

Stability Studies

The selected formulations were subjected to the accelerated stability at 30±2 °C / 65±5 % RH for 2 months and evaluated for their appearance, hardness, friability, drug content & *in-vitro* dissolution studies. There were no significant variations in the appearance, hardess, friability, drug content and *in vitro* dissolution studies.

CONCLUSION

The main objective in the relation to this study was development of a colon targeted matrix tablet formulation of Ivermectin. The intention was to prepare a formulation, by wet granulation technique using various proportion of guar gum as polymer. Eight batches were prepared with various percentage of guar gum and further coating was done using Eudragit-L 100. The formulation developed also had to prevent drug liberation at the stomach. It was found that the formulation liberation in the stomach was prevented by enteric coating but after gastric emptying drug release was adjusted by incorporation of citric acid. If citric acid is incorporated in the tablet matrix the tablet is likely to remain entire for longer period. In this way drug release at the end of the small intestine might be prevented even through pH levels exceeding 7. In the colon the formulation can disintegrate into granules. These can then distribute themselves throughout the colon. All the colon targeted matrix formulations prepared were evaluated for physicochemical parameters such as appearance, physical properties, drug content and *in-vitro* dissolution studies and stability studies. All the physical characteristics of the formulations like thickness, hardness, friability, drug content, and *in vitro* dissolution study were found to be well within the limits and official standards. Stability of the tablets at conditions 30 ±2° C / 65 ±5 % RH, was assessed and observed for appearance, hardness, friability, drug content and *in-vitro* study. From the stability studies it was found that the formulation was stable at 30 ±2 °C / 65 ±5 % RH. The susceptibility of the matrix tablets to the enzymatic action of colonic bacteria was assessed by performing the drug release studies in medium containing rat caecal material (4%). From the *in-vitro* dissolution studies it was found to be that formulation IF_1 with 7.5% guar gum, IF_2 with 15% guar gum, IF_3 with 22.5% guar gum & IF_4 with 30% guar gum were failed to retard the drug release, it might be due to the release of majority of drug within 10 h in the region of stomach & small intestine. The formulation IF_5 containing 37.5% guar gum was also failed to retard the drug release, IF_5 formulation released 93.90 % drug within 12 h and was unable to maintain the drug release through out the study period 24 h. In the presents study it was found that the formulations containing 37.5 % of guar gum was not able to target the colon in the form of colon targeted matrix tablet. *In-vitro* release data of marketed product was revealed that the single dose was unable to target the drug to colon because the marketed product releases the majority of drug within 9 h. Formulation IF_6 with 45% guar gum emerged to be the best one, because it exhibits the best overall general appearance, hardness of 5.5±0.147 Kg/cm^2, friability and a maximum percentage drug release 94.69 without rat caecal content & 98.62% with rat caecal content at the end of 24 h *in-vitro* dissolution studies. In the present study, the matrix formulation containing 45% guar gum is most likely to target Ivermectin to colon without being released significantly in stomach and small intestine.

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