Design and evaluation of Azathioprine loaded flakes in cap for Colon Specificity

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Abstract :

Colonic delivery refers to targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e. colon). Colonic delivery refers to targeted delivery of drugs in the lower GI tract, this occurs primarily in the large intestine (i.e. colon). Colonic delivery refers to targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e. colon). Colonic delivery refers to targeted delivery of drugs into the lower GI tract, which occurs primarily in the large intestine (i.e. colon). Azathioprine is an immunosuppressant, that is, a drug that is used to suppress the immune system. The present investigation concerns the development of mouth dissolving tablet of azathioprine which were designed colon specificity. flakes of azathioprine were formulated using polymers namely black mustard, yellow mustard, sorghum, ragi, pectin, guar gum carried out studies for Weight variation., Hardness., Friability, Uniformity of weight, Water absorption ratio, Wetting time, Disintegration test and *in-vitro* dissolution study.

Keywords: Colonic delivery, Azathioprine, Immunosuppressant

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Introduction

Targeted drug delivery into the colon is highly desirable or local treatment of a variety of bowel diseases such as ulcerative colitis, Crohn's disease, amebiosis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs. [1, 2] Oral delivery is the most preferred route of drug delivery due to ease of administration, patient compliance, low cost, flexibility in formulation etc. However, first pass metabolism, gastric degradation and fluctuations in drug concentration due to the influence of gastric emptying, nature of food etc are the major limitations that can be overcome by delivering the drug molecule to the site of maximum absorption. [3] Colonic drug delivery is a relatively new area that has evolved after recognition of the advantages associated with almost

neutral pH of colon for drug absorption. Absorpt ion of drugs is furtherfacilitated due to the long residence time of the dosage form in the colon. Drug absorption from colon is not affected by nature of food and enzymes, which makes it ideal for administration of peptides and hormones. [4] Targeting of drug specifically to the colon is advantageous in the treatment of various diseases such as amoebiasis, Crohn's disease, ulcerative colitis and colorectal cancer. In addition, it has shown great potential in the oral delivery of therapeutic peptides and

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proteins which are unstable in the upper part of gastro-intestinal tract (GIT). [5] Apart from protecting these labile molecules, colon also offers an opportunistic site for oral delivery of vaccines because it is rich in lymphoid tissue. A colonic targeted approach found to be effected in minimizing uncertain side effects. So the colon as a site for drug delivery offers distinct advantages on account of near neutral pH, a much longer transit time, relatively low proteolytic activity and offers a much greater responsiveness to absorption enhances. [6] This delivery system canbe also used in certain conditions where drugs should be delivered after a lag time, like in Chronopharmacotherapy of diseases showing circadian rhythms in their pathophysiology. [7] Rectal route of drug administration is also found to be shortest route for targeting drug to colon. Although approaching the proximal part of colon is not easy via rectal route of administration. Rectal administration of drug offers less compliance and is also uncomfortable for patients. [8]

Material and Methods

The biomaterial was isolated from the natural edible source. The best quality seeds of black mustard, yellow mustard, jowar, wheat, mandua) were purchased. The seeds (250gm) were soaked with 600ml distilled water overnight. The seeds were crushed to obtain seed coats. The seed coats were powdered and slurry was prepared and kept overnight and filtered to obtain the filtrate and further filtrate was treated with equal volume (1:1ratio) of acetone and finally refrigerated for 24 hrs. The s.

biomaterial was collected via centrifugation .The oil was removed by washing with chloroform and drying in desiccators for 24hrs. The biomaterial was further treated with various site specific buffers (1.2, 6.8, 3.4, and 7.4). The biomaterial was optimized six times to check the yield of the polymer. The yield was found to be 2.36 gm, 2.89gm, 1.8gm, 1.67 gm, 1.1gm.

Preparation of Azathioprine loaded flakes

Azathioprine loaded flakes were prepared by compression of various ingredients in different ratios. It included drug (Azathioprine, biomaterial, Mcc, talc and Mg.stearate) initially drug was nanosized via two methods standard method and novel method. In novel method 10 mg of drug was taken then alcoholic KOH was added along with 5microlitre of sorbitol. To this mixture water was added drop wise and further kept on magnetic stirrer for 15 minutes. The resultant solution was sonicated for 6 cycles each of 3 minutes. The solution was centrifuged supernatant and residue was dried to obtain nano sized particle of drug. Another method performed was standard method. In this method drug was mixed with the solvent alcoholic KOH. This mixture was sonicated and water was added drop wise. The water was evaporated via non evaporation method. This solution was sonicated for 6 cycles then centrifuged to obtain nano sized drug. Once drug was nanosized it was compressed in machine with various ingredients in different ratio

Table no1: **Formula for preparing Azathioprine flakes with biomaterial obtained from blackmustard.**

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FORMULATION/ CONTENT	FB1 (1:.1)	FB2 (1:0. 5	FB3 (1:0. 8)	FB4 (1:0.9)	FB5 (1:1)	FB6 (1:2)	FB7 (1:2. 5)	FB8 (1:3)	FB9 (1:3.5)	FB10 (1:4)
Azathioprine (mg)	10	10	10	10	10	10	10	10	10	10
Black mustard(mg)	1	5	8	9	10	20	25	30	35	40
Mcc(mg)	100	100	100	100	100	100	100	100	100	100
Mg.stearate(mg)	2 %	2%	2%	2%	2%	2%	2%	2%	2%	2%
Talc(mg)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%

Table no 2: Formula for Azathioprine flakes using biomaterial obtained from Black mustard

Formulation	FB11 (1:5.5)	FB12 (1:6)	FB13 (1:8)	FB14 (1:10)	FB15 (1:10.5)	FB16 (1:12)	FB17 (1:14)	FB18 (1:18)	FB19 (1:20)	FB20 (1:22)
Azathioprine	10	10	10	10	10	10	10	10	10	10
Black mustard	55	60	80	100	105	120	140	180	200	220
Mcc	100	100	100	100	100	100	100	100	100	100
Talc	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
Mg.stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%

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Table no. 3: **Formulation of Azathioprine flakes using biomaterial obtained fromwheat**.

FORMULATION/ CONTENT	FW1 (1:.2)	FW2 (1:0.4)	FW3 (1:0.6)	FW4 (1:1)	FW5 (1:4)	FW6 (1:6)	FW7 (1:8)	FW8 (1:10)	FW9 (1:15)	FW10 (1:20)	FW11 (1:.2)
Azathioprine (mg)	10	10	10	10	10	10	10	10	10	10	10
Wheat (mg)	2	4	6	10	40	60	80	100	150	200	2
Mcc(mg)	100	100	100	100	100	100	100	100	100	100	100
Mg.stearate(mg)	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
Talc(mg)	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%

Table no 4: Formulation of Azathioprine flakes using biomaterial from yellowmustard.

Formulation	FY1 (0.1)	FY2 (0.5)	FY3 (1:1)	FY4 (1:2)	FY5 (1:4)	FY6 (1:6)	FY7 (1:8)	FY8 (1:10)	FY9 (1:11)	FY10 (1:15)	FY11 (1:20)
Azathioprine	10	10	10	10	10	10	10	10	10	10	10
Yellow mustard	1	5	10	20	40	60	80	100	110	150	200
Mcc	100	100	100	100	100	100	100	100	100	100	100
Talc	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
Mg.stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%

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Table no 5: Formulation of Azathioprine flakes using biomaterial obtained from jowar.

Formulation	FJ1 (1:0.1)	FJ2 (1:0.5)	FJ3 (1:1)	FJ4 (1:2)	FJ5 (1:4)	FJ6 (1:4.5)	FJ7 (1:5)	FJ8 (1:6)	FJ9 (1:8)	FJ10 (1:10)
Azathioprine	10	10	10	10	10	10	10	10	10	10
Jowar	1	5	10	20	40	45	50	60	80	100
Mcc	100	100	100	100	100	100	100	100	100	100
Mg.stearate	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
Talc	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%

Formulation	FJ11 (1:12)	FJ12 (1:18)	FJ13 (1:20)
Azathioprine	10	10	10
Jowar	120	180	200
Mcc	100	100	100
Mg.stearate	2%	2%	2%
Talc	1%	1%	1%

Table no. 6: Formulation of Azathioprine flakes using biomaterial obtained frommandua.

Formulation	FM1 (1:0.5)	FM2 (1:0.8)	FM3 (1:1)	FM4 (1:2)	FM5 (1:2.5)	FM6 (1:2.8)	FM7 (1:3)	FM8 (1:4)	FM9 (1:8)	FM10 (1:9)
Azathioprine	10	10	10	10	10	10	10	10	10	10
Mandua	5	8	10	20	25	28	30	40	80	90

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Mcc	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**
Mg.stearate	**2%**	**2%**	**2%**	**2%**	**2%**	**2%**	**2%**	**2%**	**2%**	**2%**
Talc	**1%**	**1%**	**1%**	**1%**	**1%**	**1%**	**1%**	**1%**	**1%**	**1%**

Table no.7: Formulation of Azathioprine flakes using standard polymer pectin.

Formulation	**FP1 (1:0.9)**	**FP2 (1:1)**	**FP3 (1:3)**	**FP4 (1:5.5)**	**FP5 (1:6)**	**FP6 (1:12)**	**FP7 (1:14)**	**FP8 (1:22)**
Azathioprine	10	10	10	10	10	10	10	10
Pectin	9	10	30	55	60	120	140	220
Mcc	100	100	100	100	100	100	100	100
Mg.stearate	2%	2%	2%	2%	2%	2%	2%	2%
Talc	1%	1%	1%	1%	1%	1%	1%	1%

Table no. 8: Formulation of Azathioprine flakes using standard polymer guar gum.

Formulation	**FG1 (1:2)**	**FG2 (1:4)**	**FG3 (1:10)**	**FG4 (1:10.5)**	**FG5 (1:18)**	**FG6 (1:20)**	**FG7 (1:25)**
Azathioprine	10	10	10	10	10	10	10
Guar gum	20	40	100	105	180	200	250
Mcc	100	100	100	100	100	100	100
Mg.stearate	2%	2%	2%	2%	2%	2%	2%
Talc	1%	1%	1%	1%	1%	1%	1%

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EVALUATION OF THE FORMULATED FLAKES

The prepared formulations are subjected for various evaluation parameters such as drug content uniformity, Entrapment efficiency, % transmittance, particle size, particle shape, *in-vitro* drug release.

DRUG CONTENT UNIFORMITY:

A novel carrier system should allow a high loading capacity or drug content uniformity for the incorporated drugs and provide long term incorporation. This can be generally expressed in percent related to lipid phase (lipid + drug)

$$\text{Drug content uniformity (\%)} = \frac{\text{Total wt. of drugs} - \text{wt. of free drug}}{\text{Total wt. of drugs}} * 100$$

For the evaluation of drug content uniformity, drug loaded flakes (100 mg) were powdered and suspended in 10 ml of alcoholic KOH solvent. The resultant dispersion was kept for 20 min for complete mixing with continuous agitation in the sonicator and filtered through a 0.45 µm membrane filter. This sample was kept overnight. The drug content was determined spectrophotometrically by UV apparatus at 280 nm using a regression equation derived from the standard graph (m= 0.070). All the experimental units were analyzed triplicate.

INVITRO DRUG RELEASE:

Invitro drug release was carried out by following apparatus:.

1. Modified M S Diffusion cell by static method:

The drug release was performed by using egg shell membrane, which was separated out by dissolving egg in conc. HCl, This egg shell membrane was tied to one end of broken tubes which act as doner compartment. Flakes loaded with Azathioprine was applied in the membrane in the donor compartment containing buffer 3.4, which was attached to another plastic bottle in such a way that the egg membrane touches the receptor

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compartment containing of Ph 7.4 buffer which serves as the receptor compartment. The assembly was set up in a thermacol which act as thermostat and the temperature was maintained at 37°C. At each interval of time the sampling was done from the bottle containing 3.4 buffer. At different interval of time the assembly was completely replaced. This method for Ph 3.4 buffer was done till 36 Hrs. The samples were then subjected to analysis by UV Spectroscopy.

Stability Studies for the best formulation:

Stability studies were conducted as per ICH guidelines. The stability studies of selected formulation (FA6) was conducted at various condition of temperature and relative humidity. The selected formulation was kept for stability studies for 3 months at different temperature:

- In an oven, at 40 °C
- In refrigerator at 4-8°C
- At room temperature

And weekly observation was carried out for any changes in physicochemicalproperties *In-vitro* drug release, drug content uniformity, and transmittance & entrapment efficiency.

RESULT AND DISCUSSION

Spectral studies of isolated biomaterial

Drug –polymer interaction studies using ultraviolet spectroscopy

The absorbance of pure drug was observed as 0.114 at 320nm.then absorbance`s of 1:1,3:1,1:3,1:20 drug polymer ratio were observed Then wavelength and absorbance of drug-biopolymer ratios (1:1, 3:1 1:20 and 1:3) were observed a λmax 320nm. There was found no change in maximum wavelength and absorbance of drug and drug-biopolymer ratios. So biopolymer is not reactive with functional group of drug and inert in nature. So biopolymer can be used for further formulation of flakes.

SEM analysis of isolated biopolymer

From the SEM imaging of isolated biopolymer (black mustard) it can be seen that it`s crystalline and irregular in shape with rough and shiny texture that was similar to natural polymer.

Preparation of Standard curve of Azathioprine at phosphate buffer 7.4

From the standard graph of Azathioprine, slope was calculated as and R^2 value as

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and that was used for calculating drug release data.

Formulation of Azathioprine flakes using isolated biopolymer

The Azathioprine loaded flakes was prepared using isolated biopolymer.

The bio-material obtained from various sources were used. For the formulation polymer and drug was taken in equal ratio added 5 micro litre of sorbitol. 5ml of distil water was

added dropwise then kept on magnetic stirrer for 5 min further sonicated for 8 cycles 3times then centrifuged to obtain supernatant and sediment. Both were dried.

Formulation of bio flakes using standard polymers

Two different synthetic polymer guar gum and pectin were selected as standard polymer based on their good suspending property for preparation of flakes. The prepared flakes in different drug – polymer ratio was found to be reproducible and further subjected to various evaluation parameters. Their results were compared with the results of isolated biopolymer parameters.

Evaluation of formulated bio flakes pH

Measurement

The pH was obtained in the range of 7.2 to 7.4, 0.10±0.20 for flakes using *black mustard* biopolymer.

The pH was obtained in the range of 7.0 to 7.5, 0.25±0.05 for flakes using *yellow mustard* biopolymer.

The pH was obtained in the range of 7.1 to 7.5, 0.11±0.04 for flakes using *mandua* biopolymer

The pH was obtained in the range of 7.0 to 7.5, 0.25±0.05 for flakes using *wheat* biopolymer

The pH was obtained in the range of 7.0 to 7.5, 0.25±0.05 for flakes using *jowar* biopolymer

The pH was obtained in the range of 7.0 to 7.5, 0.35±0.05 for flakes using standard polymer. pH value of all formulations is in the range of physiological pH, so prepared flakes is suitable for oral administration.

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RELEASE KINETIC ANALYSIS DYNAMIC METHOD

Formulation of Black mustard

FORMULATION(black Mustard)	**ZERO ORDER (R^2)**	**FIRST ORDER(R^2)**	**H.MATRIX(R^2)**	**PEPPAS (R^2)**	**HIX.CROW (R^2)**	**BEST FIT MODEL**	**MECH. OF RELEASE**
1:1	.5084	.8671	.7876	.9056	.7418	Peppas Korsmeyer	Anomalos Transport
1:2	.4925	.8317	.7784	.8884	.7115	Peppas Korsmeyer	Anomalos Transport
1:3	.4647	.8296	.7608	.8909	.6992	Peppas Korsmeyer	Fickian diffusion
1:3.5	.4629	.8235	.7589	.8882	.6983	Peppas Korsmeyer	Fickian diffusion
1:4	.4705	.8304	.7618	.8910	.7011	Peppas Korsmeyer	Fickian diffusion
1:6	.4621	.8053	.7688	.8971	.7097	Peppas Korsmeyer	Fickian diffusion
1:8	.4748	.8382	.7688	.8971	.7097	Peppas Korsmeyer	Fickian diffusion
1:10	.4806	.8449	.7727	.8968	.7175	Peppas Korsmeyer	Fickian diffusion
1:12	.4698	.8211	.7650	.9023	.6959	Peppas Korsmeyer	Fickian diffusion
1:14	.4582	.8274	.7555	.8912	.6945	Peppas Korsmeyer	Fickian diffusion

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FORMULATION(black Mustard)	ZERO ORDER (R^2)	FIRST ORDER (R^2)	H.MATRIX (R^2)	PEPPAS (R^2)	HIX.CROW (R^2)	BEST FIT MODEL	MECH. OF RELEASE
1:18	.4641	.8111	.7593	.8830	.6868	Peppas Korsmeyer	Fickian diffusion
1:20	.4494	.8076	.7489	.8860	.6780	Peppas Korsmeyer	Fickian diffusion
1:22	.4403	.8235	.7410	.8837	.6832	Peppas Korsmeyer	Fickian diffusion
1:0.1	.4632	.8363	.7570	.8963	.7009	Peppas Korsmeyer	Fickian diffusion
1:0.5	.4664	.8518	.7620	.8913	.7149	Peppas Korsmeyer	Fickian diffusion
1:0.8	.4529	.8234	.7513	.8843	.6908	Peppas Korsmeyer	Fickian diffusion
1:0.9	.4543	.8359	.7525	.8836	.6985	Peppas Korsmeyer	Fickian diffusion
1:2.5	.4606	.8679	.7583	.9002	.7237	Peppas Korsmeyer	Fickian diffusion
1:5.5	.4582	.8353	.7556	.8931	.6994	Peppas Korsmeyer	Fickian diffusion
1:10.5	.4577	.8424	.7543	.8876	.7034	Peppas Korsmeyer	Fickian diffusion

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RELEASE KINETIC ANALYSIS BY DYNAMIC METHOD

Formulation of jowar

FORMULATION Jowar	ZERO ORDER (R^2)	FIRST ORDER (R^2)	H.MATRIX (R^2)	PEPPAS (R^2)	HIX.CROW (R^2)	BEST FIT MODEL	MECH. OF RELEASE
1:1	.4843	.7680	.7746	.8904	.6674	Peppas Korsmeyer	Fickian diffusion
1:2	.4917	.7682	.7796	.8944	.6702	Peppas Korsmeyer	Anomalous Transport
1:4	.5209	.7957	.7974	.9084	.6997	Peppas Korsmeyer	Anomalous Transport
1:5	.4939	.7874	.7798	.8918	.6830	Peppas Korsmeyer	Anomalous Transport
1:6	.5016	.7849	.7848	.9032	.6844	Peppas Korsmeyer	Anomalous Transport
1:8	.5148	.8148	.7959	.9019	.7104	Peppas Korsmeyer	Anomalous Transport
1:10	.5090	.8033	.7927	.9031	.7007	Peppas Korsmeyer	Anomalous Transport
1:12	.4901	.7680	.7788	.8969	.6697	Peppas Korsmeyer	Fickian diffusion
1:18	.4962	.7787	.7823	.9025	.6787	Peppas Korsmeyer	Anomalous Transport
1:20	.5160	.8062	.7957	.9013	.7048	Peppas Korsmeyer	Anomalous Transport
1:.1	.4839	.7839	.7730	.8890	.6767	Peppas Korsmeyer	Anomalous Transport
1:.5	.5008	.8118	.7860	.8928	.7026	Peppas Korsmeyer	Anomalous Transport
1:4.5	.5354	.8137	.8081	.9183	.7178	Peppas Korsmeyer	Anomalous Transport

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RELEASE KINETIC ANALYSIS BY DYNAMIC METHOD

Formulation of wheat

FORMULATION (wheat)	ZERO ORDER (R^2)	FIRST ORDER (R^2)	H.MATRIX (R^2)	PEPPAS(R^2)	HIX.CROW (R^2)	BEST FIT MODEL	MECH. OF RELEASE
1:1	.5193	.8030	.7975	.8979	.7092	Peppas Korsmeyer	Anomalous Transport
1:4	.5062	.8178	.7915	.8924	.7096	Peppas Korsmeyer	Anomalous Transport
1:6	.5070	.8088	.7925	.9030	.7042	Peppas Korsmeyer	Fickian diffusion
1:8	.5043	.7963	.7873	.9044	.6936	Peppas Korsmeyer	Anomalous Transport
1:10	.5156	.8227	.7948	.8991	.7156	Peppas Korsmeyer	Anomalous Transport
1:20	.5051	.8241	.7895	.9011	.7128	Peppas Korsmeyer	Anomalous Transport
1:0.5	.5062	.8059	.7888	.8893	.7006	Peppas Korsmeyer	Anomalous Transport
1:0.2	.5344	.8423	.8081	.9027	.7372	Peppas Korsmeyer	Anomalous Transport
1:0.4	.5174	.8130	.7960	.8984	.7098	Peppas Korsmeyer	Anomalous Transport
1:15	.5195	.8308	.7973	.8961	.7228	Peppas Korsmeyer	Anomalous Transport

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RELEASE KINETIC ANALYSIS BY DYNAMIC METHOD

Formulation of yellow mustard

FORMULATION Yellow Mustard)	ZERO ORDER (R^2)	FIRST ORDER (R^2)	H.MATRIX (R^2)	PEPPAS (R^2)	HIX.CROW (R^2)	BEST FIT MODEL	MECH. OF RELEASE
1:1	.5160	.7962	.7964	.9019	.6984	Peppas Korsmeyer	Anomalous Transport
1:2	.4959	.7933	.7826	.8982	.6881	Peppas Korsmeyer	Anomalous Transport
1:4	.5285	.8190	.8046	.9164	.7187	Peppas Korsmeyer	Anomalous Transport
1:6	.5038	.8020	.7874	.9053	.6968	Peppas Korsmeyer	Anomalous Transport
1:8	.5282	.8223	.8049	.8984	.7212	Peppas Korsmeyer	Anomalous Transport
1:10	.5331	.8196	.8061	.8995	.7204	Peppas Korsmeyer	Anomalous Transport
1:20	.5288	.8276	.8049	.9020	.7248	Peppas Korsmeyer	Anomalous Transport
1:0.1	.5358	.8335	.8107	.9004	.7321	Peppas Korsmeyer	Anomalous Transport
1:0.5	.5190	.8348	.7992	.8944	.7258	Peppas Korsmeyer	Anomalous Transport
1:15	.5519	.8389	.8203	.9140	.7421	Peppas Korsmeyer	Anomalous Transport
1:11	.5194	.8235	.7988	.9085	.7179	Peppas Korsmeyer	Anomalous Transport

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RELEASE KINETIC BY DYNAMIC METHOD

Formulation of pectin

FORMULATION (Pectin)	ZERO ORDER (R^2)	FIRST ORDER (R^2)	H.MATRIX (R^2)	PEPPAS (R^2)	HIX.CROW (R^2)	BEST FIT MODEL	MECH. OF RELEASE
1:1	.5425	.8686	.8116	.9099	.7582	Peppas Korsmeyer	Anomalous Transport
1:3	.5156	.8519	.7969	.9030	.7363	Peppas Korsmeyer	Anomalous Transport
1:6	.5466	.8602	.8168	.9161	.7550	Peppas Korsmeyer	Anomalous Transport
1:12	.5230	.8542	.8005	.9114	.7403	Peppas Korsmeyer	Anomalous Transport
1:14	.5198	.8458	.7984	.9029	.7332	Peppas Korsmeyer	Anomalous Transport
1:22	.5114	.8250	.7939	.9069	.7159	Peppas Korsmeyer	Anomalous Transport
1:0.9	.5137	.8220	.7961	.9038	.7153	Peppas Korsmeyer	Anomalous Transport
1:5.5	.5090	.8216	.7930	.8978	.7128	Peppas Korsmeyer	Anomalous Transport

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RELEASE KINETIC ANALYSIS BY DYNAMIC METHOD

Formulation of guar gum

FORMULATION (guar gum)	ZERO ORDER (R^2)	FIRST ORDER (R^2)	H.MATRIX (R^2)	PEPPAS (R^2)	HIX.CROW (R^2)	BEST FIT MODEL	MECH. OF RELEASE
1:2	.5240	.8688	.8004	.9152	.7509	Peppas Korsmeyer	Anomalous Transport
1:4	.5248	.8358	.8025	.9139	.7287	Peppas Korsmeyer	Anomalous Transport
1:10	.5104	.8413	.7937	.9033	.7266	Peppas Korsmeyer	Anomalous Transport
1:18	.5235	.8540	.8014	.9092	.7408	Peppas Korsmeyer	Anomalous Transport
1:20	.5213	.8506	.8000	.8937	.7376	Peppas Korsmeyer	Anomalous Transport
1:25	.5310	.8510	.8085	.8942	.7430	Peppas Korsmeyer	Anomalous Transport
1:10.5	.5213	.8549	.7998	.9096	.7404	Peppas Korsmeyer	Anomalous Transport

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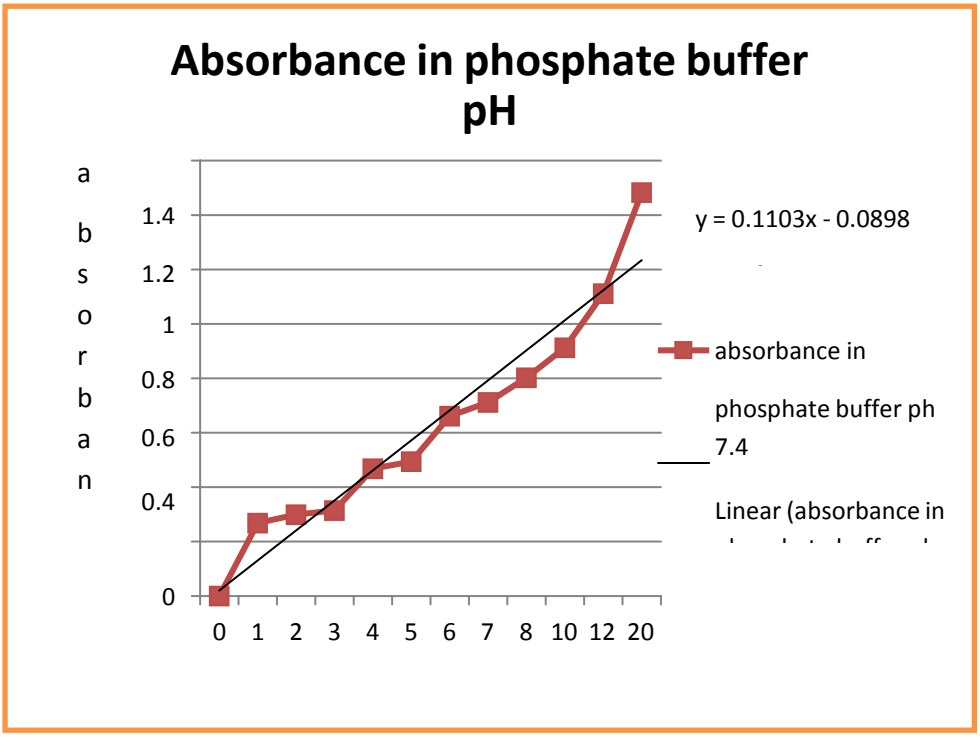
Standard curve for Azathioprine in ph 7.4



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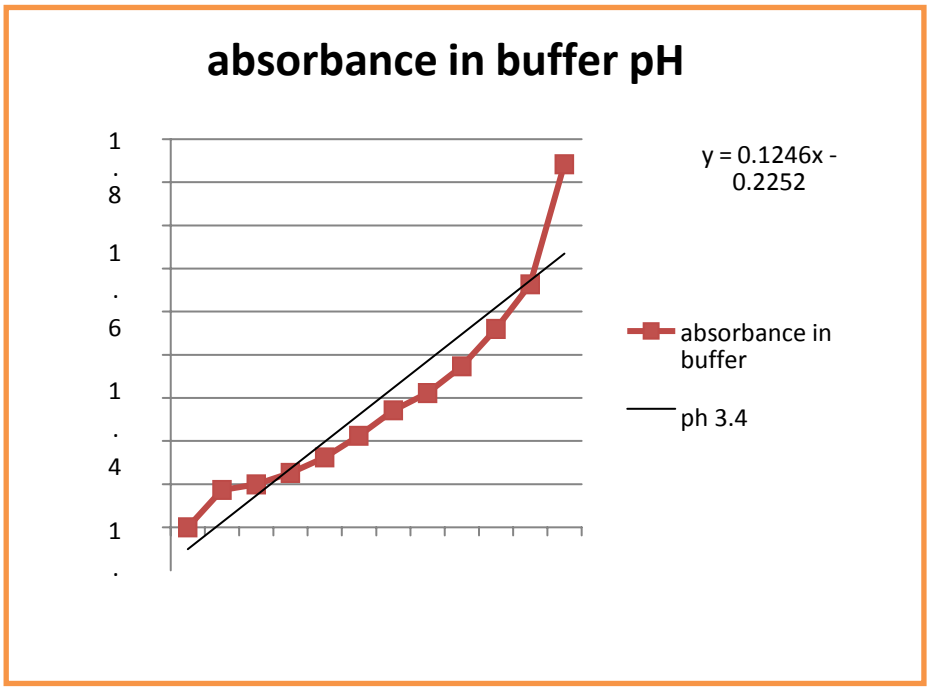
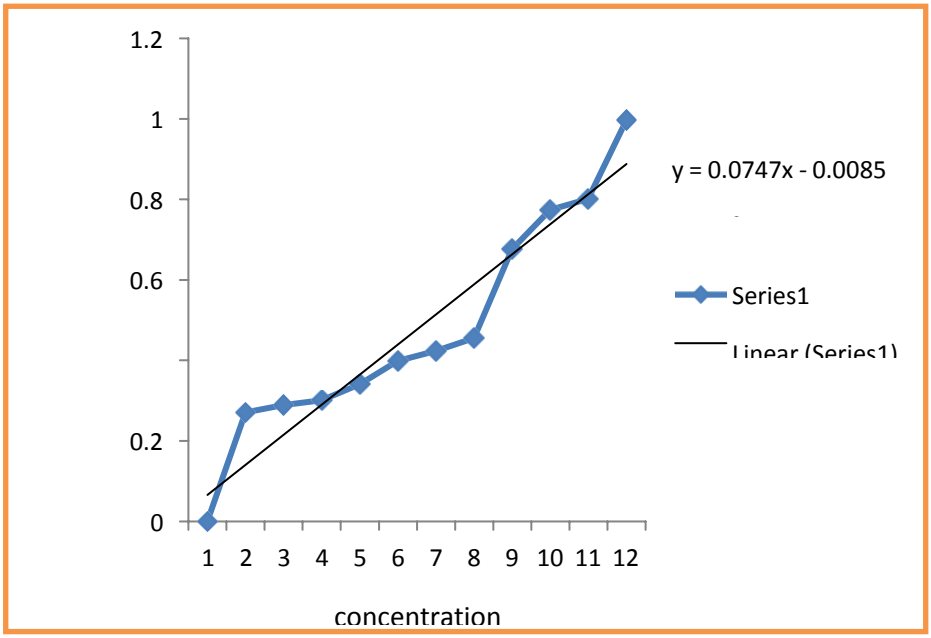


ABSORBANCE IN SOLVENT (ALCOHOLIC KOH)



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REPORTS FOR T50 AND T80 READING

BLACK MUSTARD

FORMULATION	T50	T80	FORMULATION	T50	T80
FB1	5.5	2.3	FB11	2.4	5.5
FB2	5.4	2.5	FB12	2.4	5.5
FB3	2	5.5	FB13	2.1	5.5
FB4	2.5	5.4	FB14	1.5	5.2
FB5	3.3	6	FB15	2.5	5.3
FB6	3.1	5.9	FB16	2.3	5.5
FB7	2.5	5.3	FB17	2.1	5.5
FB8	2.5	5.6	FB18	2.5	5.6
FB9	2.5	5.1	FB19	2.3	5.5
FB10	3.1	5.5	FB20	2.2	5.5

YELLOW MUSTARD

FORMULATION	T50	T80
FY1	3.7	6.2
FY2	3.5	6.0
FY3	3.5	6.5
FY4	3.4	6.2
FY5	3.5	6.1
FY6	3.6	6.0
FY7	3.6	6.3
FY8	3.7	6.5
FY9	3.5	6.1
FY10	3.9	6.3
FY11	3.6	6.3

JOWAR

FORMULATION	T50	T80
FJ1	3.4	6.2
FJ2	3.4	6.1
FJ3	3	6
FJ4	3.1	5.9
FJ5	3.5	6.3
FJ6	4.1	6.3
FJ7	3	6.1
FJ8	3	6
FJ9	3.3	6.2
FJ10	3.4	6.1
FJ11	3	6
FJ12	3.1	5.9
FJ13	3.3	6.0

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WHEAT

FORMULATION	T50	T80
FW1	3.6	6.4
FW2	3.1	5.9
FW3	3.4	6.2
FW4	3.6	6.1
FW5	3.5	6.0
FW6	6.4	9
FW7	3.5	6.4
FW8	3.5	6.4
FW9	6.5	9.3
FW10	3.3	6.3

MANDUA

FORMULATION	T50	T80
FM1	6.3	9.0
FM2	6.6	8.8
FM3	6.6	9.3
FM4	6.4	9.1
FM5	6.5	9.0
FM6	6.3	8.6
FM7	6.5	9.0
FM8	6.4	8.9
FM9	6.3	8.8
FM10	6.4	9.0

PECTIN

FORMULATION	T50	T80
FP1	3	6
FP2	6.6	8.9
FP3	3.3	6
FP4	3.2	6.4
FP5	6.7	9.0
FP6	3.3	6.1
FP7	3.4	6.4
FP8	3.5	6.2

GUAR GUM

FORMULATION	T50	T80
FG1	3.4	6.0
FG2	3.3	6.3
FG3	3.5	6.1
FG4	4.4	6.9
FG5	3	5.9
FG6	3.3	6
FG7	3.5	6.7

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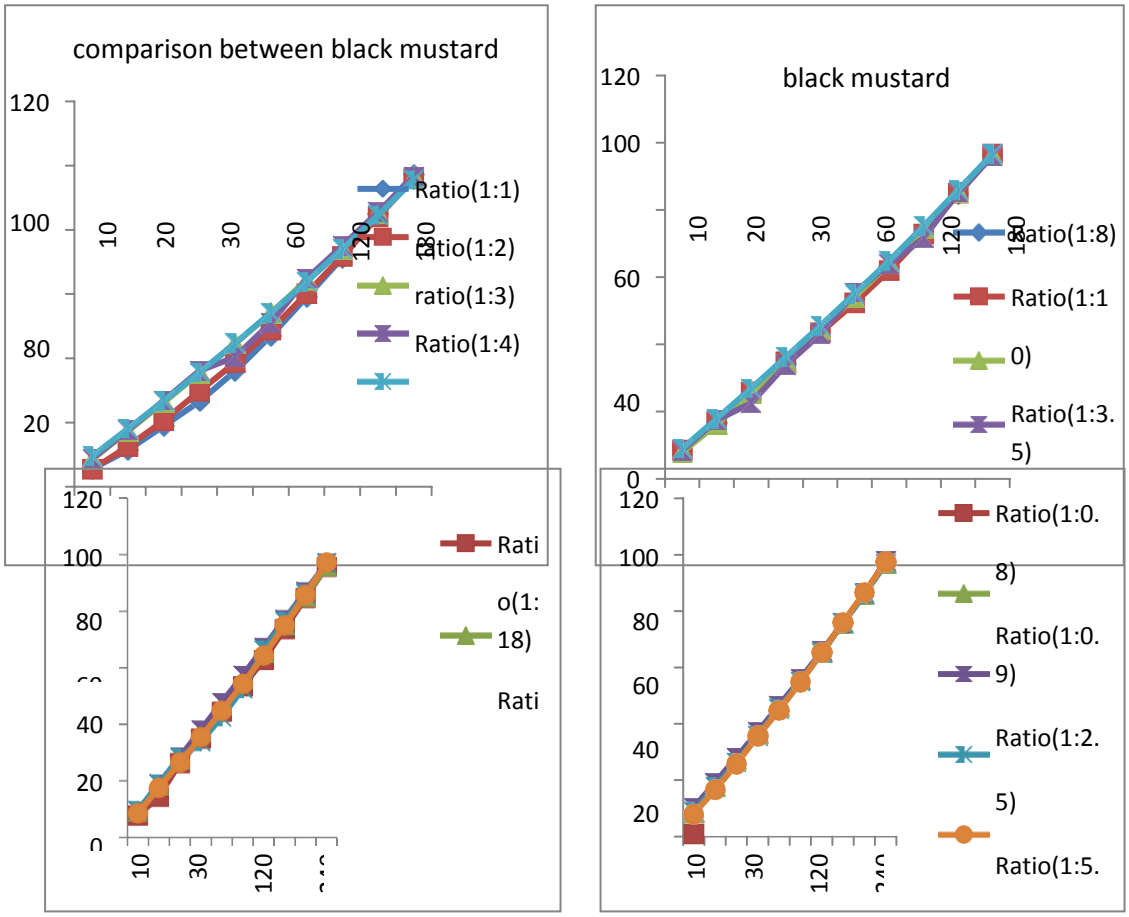
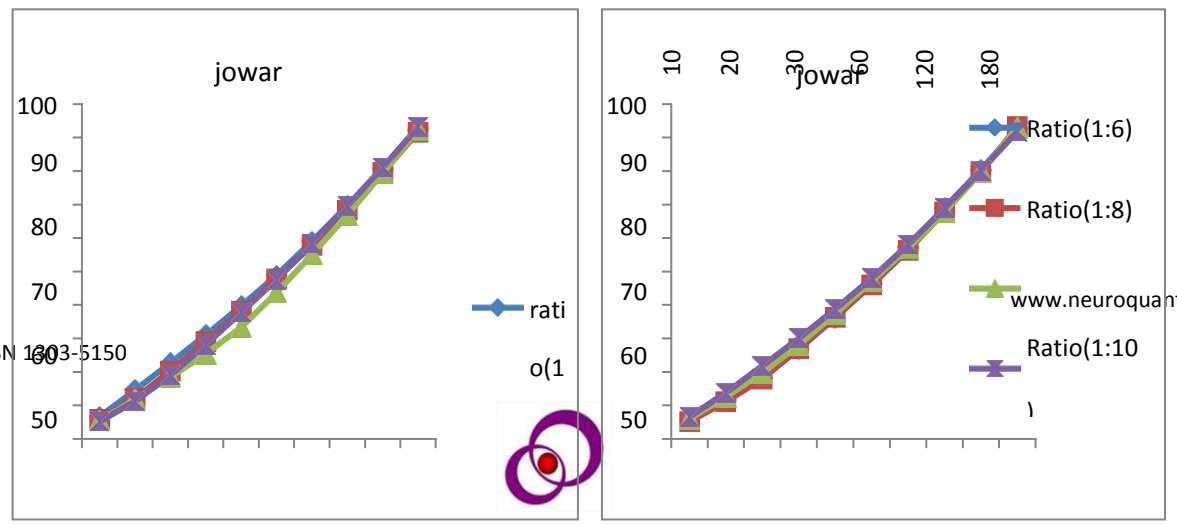
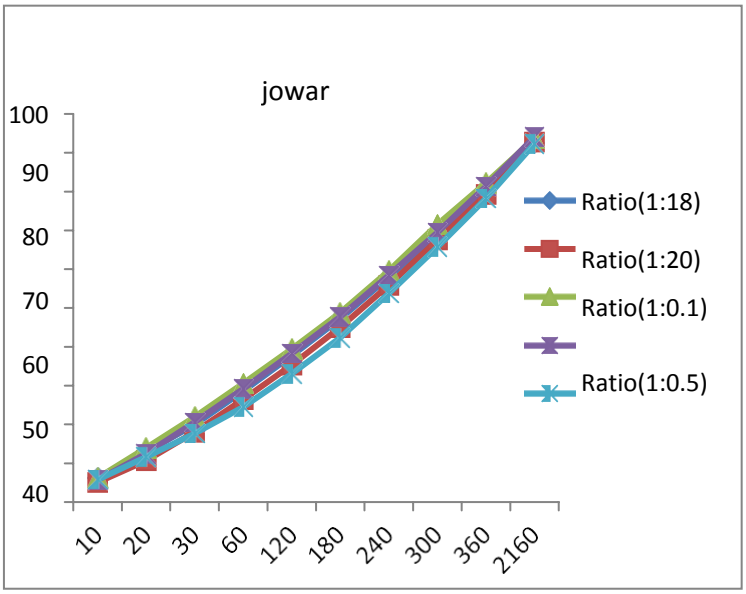
IN-VITRO DRUG RELEASE OF BLACK MUSTARD



INVITRO % DRUG RELEASE OF JOWAR





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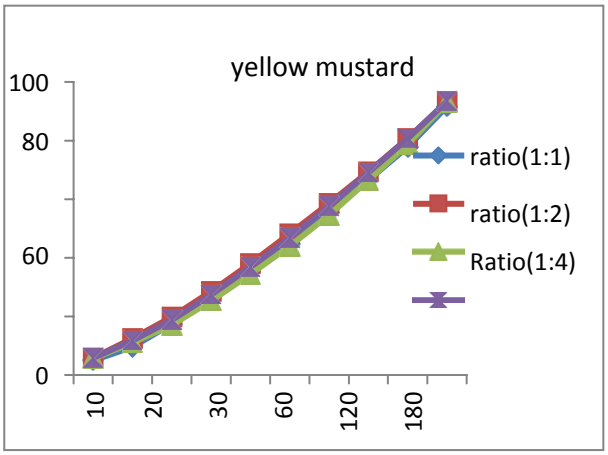
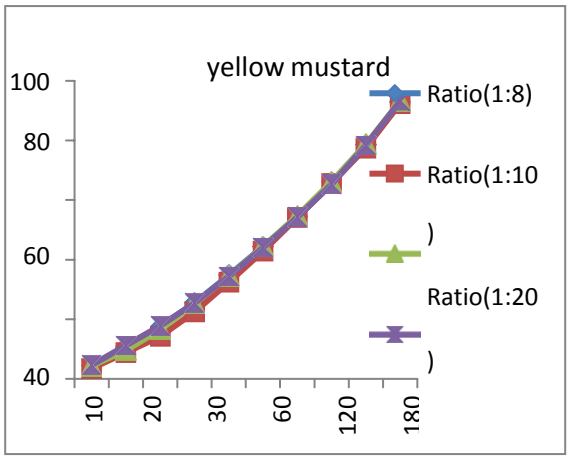
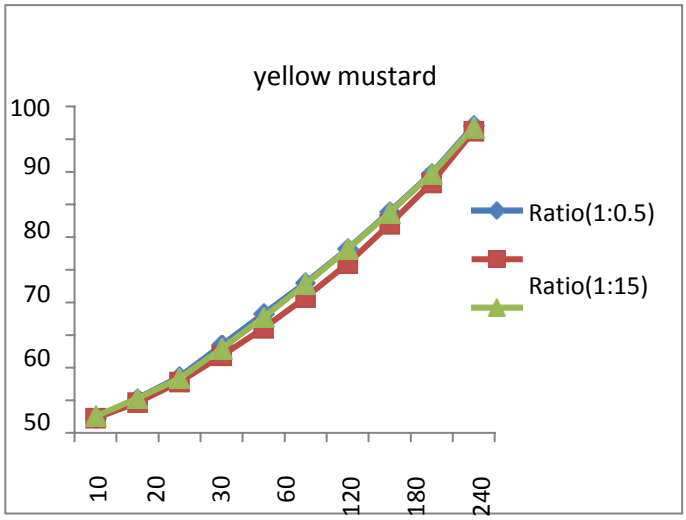
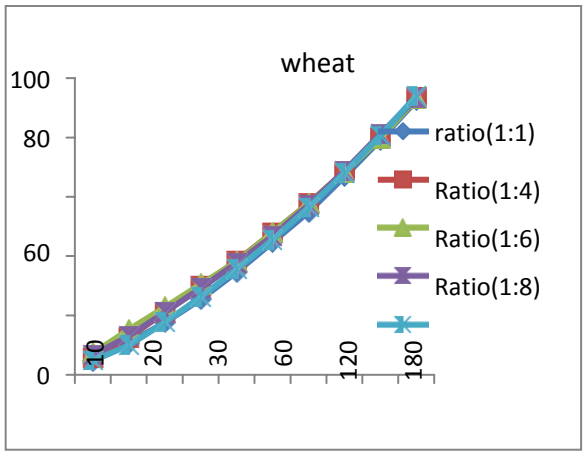
INVITRO % DRUG RELEASE OF YELLOW MUSTARD

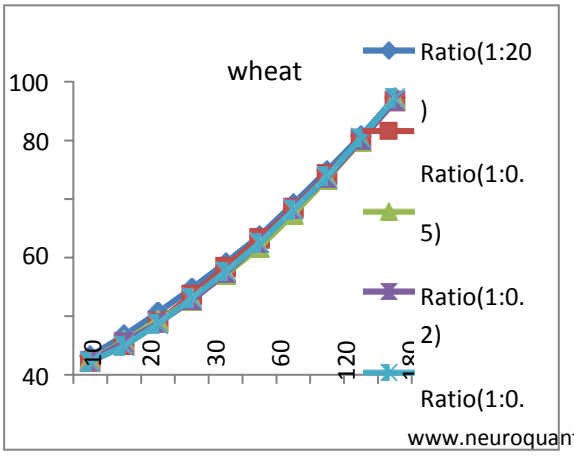






INVITRO % DRUG RELEASE OF WHEAT





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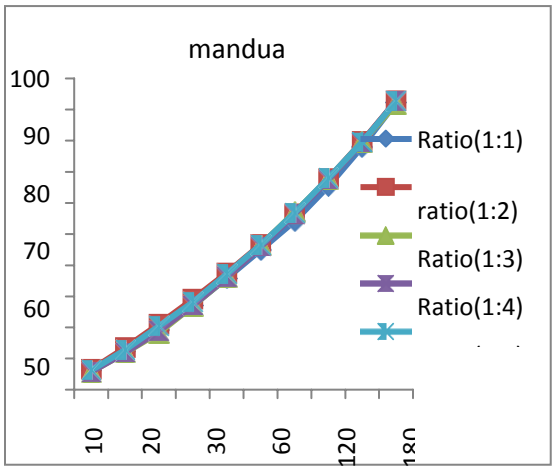
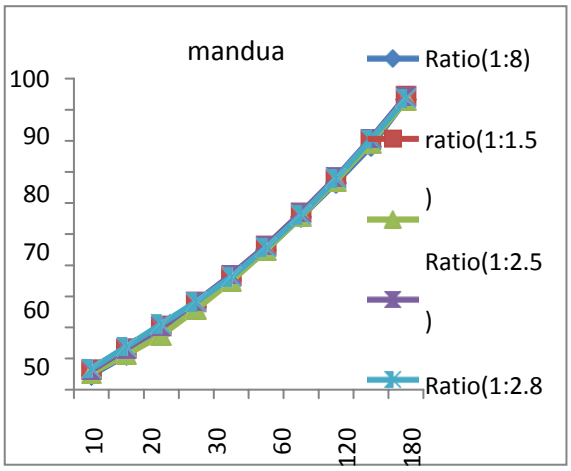
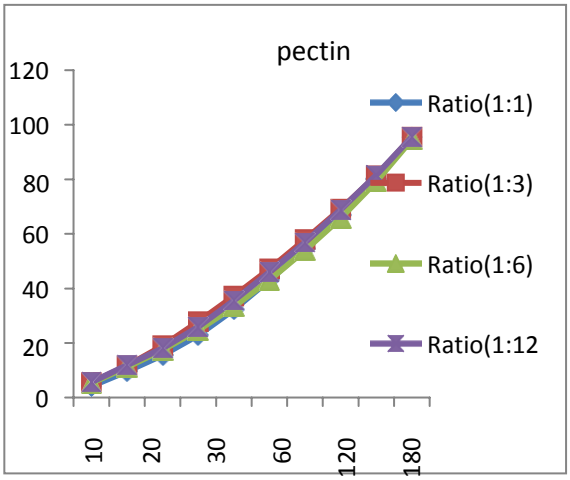
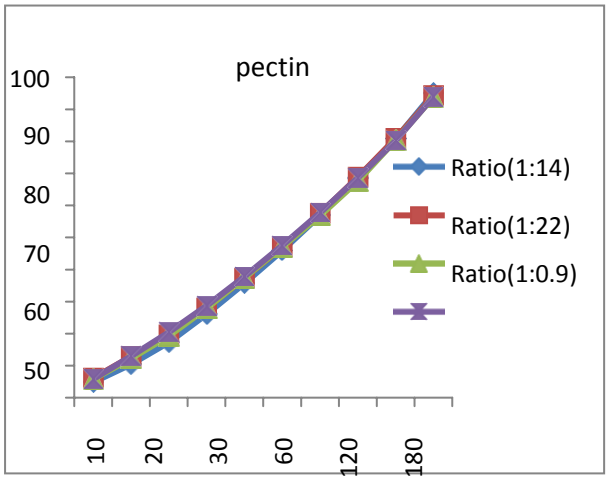
INVITRO % DRUG RELEASE OF MANDUA



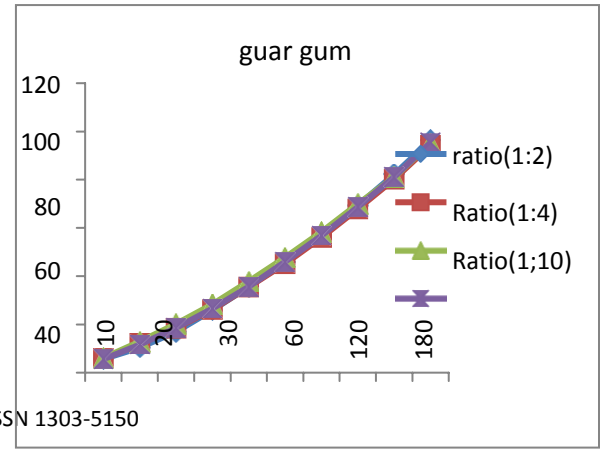


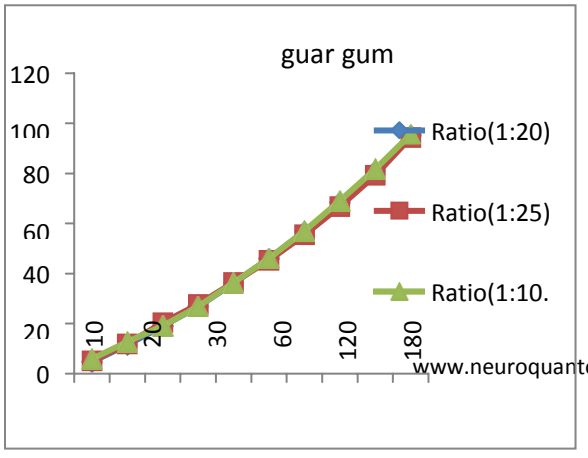
INVITRO % DRUG RELEASE OF PECTIN





INVITRO % DRUG RELEASE OF GUAR GUM





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CONCLUSION

The present study was aimed to develop colon targeted drug delivery system for delivery of Azathioprine loaded flakes. An attempted was to design Azathioprine flakes. Flakes using various natural polymers in different ration. The release of drug to be dependent on the nature and concentration of polymer used.

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