Research Article **CODEX: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

A RESEARCH ARTICLE ON FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF OXPRENOLOL HYDROCHLORIDE

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ABSTRACT

Drug delivery systems are methods which are used to ensure that drugs get into the body and reach the area where they are needed. Extended Release dosage forms are formulated in such manner as to make the contained drug available over an extended period of time following administration. Sustained release tablets are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect. Present study was to evaluate the effect of natural gums like Carrageenan, Oryza Sativa and Gum Arabic in the formulation on the in vitro dissolution of Oxprenolol Hydrochloride sustained release tablet.

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KEYWORDS

Extended release, Sustained release, Oxprenolol, Carrageenan, Oryza Sativa and Gum Arabic.

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INTRODUCTION

Oral drug delivery has been the most widely utilized route of administration among the all route because of certain advantages such as unit dosage form, low cost, cheapest for packaging etc. In the last two decades the drug delivery technology has developed rapidly and many novel oral drug delivery systems have been invented. Apart from these advantages this route suffers from certain drawbacks like patient noncompliance, multiple dosing and therapeutic failures. In order to overcome these drawbacks of conventional drug delivery there is a need for

development of new drug delivery system or modified drug delivery system. Sustained release system is a type of modified drug delivery system that can be used as an alternative to conventional drug delivery system. These systems sustain the release of drug and maintain the plasma drug concentration in therapeutic window except any fluctuation and increase the therapeutic efficacy of drug. They show their action by avoiding peak and trough in dosing and show constant plasma drug concentration in therapeutic window. Sustained release system have benefits like patient compliance, avoid multiple dosing, increase the plasma drug concentration, avoid side effects and overcome the problems associated with conventional system. Hypertension is a common disorder indicated by chronic increase in blood pressure. Hypertension prevalence has been increasing and an estimated 972 million people in the world are suffering from this problem. Incidence rates of hypertension range between 3% and 18%, depending on the age, gender, ethnicity and body size of the population. The estimated total number of adults with hypertension in 2000 was 972 million; 333 million in economically loped countries and 639million in economically developing countries. Despite advances in hypertension treatment, control rates continue to be suboptimal. Hypertension is the leading cause of cardiovascular disease worldwide. A sustained release formulation is always helpful to achieve a steady state plasma concentration for longer period of time.

MATERIALS AND METHODS

Oxprenolol Hydrochloride, Oryza sativa, Gum Arabic, Carrageenan, Lactose, Talc and Magnesium stearate.

EXPERIMENTAL METHODS

Preformulation Studies

Preformulation can be defined as an investigation of physical and chemical properties of a drug substance alone. The overall objective of preformulation studies is to generate information useful to the formulator in developing stable and bioavailable dosage forms.

Organoleptic properties
Hygroscopicity
Bulk density
Tapped density
Carr's Index
Angle of repose
Solubility
Drug- Excipient Compatibility Studies.

Preparation of Oxprenolol Hydrochloride sustained release matrix tablets

Tablets were prepared by direct compression process. Different batches of tablets, F1 to F12 were prepared by varying the concentration. The drug, Carrageenan, Gum Arabic, Oryza sativa and Talc were mixed for 10 min. Dried granules were sieved through #20, to get compressible granules. Lubricants were added during blending. During blending total mass was taken in laboratory designed small drum blender machine for about 30min. Particular attention was given to ensure uniform mixing and phase homogenization. The appropriate amounts of the mixture were accurately weighed with an electronic balance for the preparation of each tablet and finally compressed using cadmach, tablet punching machine, with a 9 mm punch. All the preparations were stored in airtight containers at room temperature for further study.

Post compression parameters

All the prepared matrix tablets were evaluated for the following official and unofficial parameters.

Details of dissolution test

Dissolution test apparatus	: USP XX II (DTD – 06P)
Speed	: 75 rpm
Stirrer	: Paddle type
Volume of medium	: 900 ml
Volume withdrawn	: 1 ml
Medium used	: 0.1 N HCl
Temperature	: 37 ± 0.5^0C
λ max:	:273nm

RESULTS AND DISCUSSION

PREFORMULATION STUDIES OF OXPRENOLOL HYDROCHLORIDE

Preformulation studies Oxprenolol Hydrochloride were done and results tabulated in Table No.2.

DRUG-EXCIPIENT COMPATIBILITY STUDIES BY FT-IR

Compatibility studies were performed using FT-IR spectrophotometer. The IR spectrum of pure drug and physical mixture of drug and polymer were studied by making a KBr disc. The characteristic absorption peaks of Oxprenolol Hydrochloride were obtained at different wave numbers in different samples.

From the spectra of pure drug Oxprenolol Hydrochloride and the combination of drug with polymers, it was observed that all the characteristic peaks of Oxprenolol Hydrochloride were present in the combination spectrum, thus indicating compatibility of the drug and polymer. IR spectra of the pure drug in combination with the polymers are shown in Figure No.1,3.

Physico chemical parameters of prepared natural polymers

Physico chemical properties of all natural polymers were studied and results were tabulated in Table No.3.

EVALUATION TESTS FOR PRE and POST COMPRESSION PARAMETERS

Pre compression parameters like Bulk density, Tapped density, Carrs index (%), Hausner's ratio and Angle of repose were studied and tabulated in Table No.4 and post compression results were tabulated in Table No.5,6.

Stability Studies

Stability studies of best formulation (F2) carried out at 40^0C and 75% RH were performed and results tabulated in Table No.7.

Summary

The present study was under taken to formulate and evaluate the sustained release matrix tablets of Oxprenolol Hydrochloride using natural polymers. The study involved the selection of natural polymers like Carrageenan, Gum Arabic, Oryza Sativa for slow release of drug and for extended action of the drug. Preformulation studies of drug and excipients shown that there is no interaction between the API and the polymers used.

The *In-vitro* drug release was studied in USP XXII dissolution apparatus in 0.1 N HCl for 12 hrs. The results shown that the all the formulations of direct compression matrix tablets shown the good release of the drug from the formulations. In case of direct compression matrix tablets F2, the release of drug shows 99.37 and controlled the drug release. So, the formulation F2 is suited for the extended release of Oxprenolol Hydrochloride in the treatment of Hypertension.

The viscosity of Gum Arabic is more than the Carrageenan and it causes the slower drug release than the Carrageenan based matrix tablets. So, the viscosity of the polymer also controls the release of the drug from the matrix tablets.

In release kinetic study the 'n' value ranges from 0.983 to 0.999 for all formulations, these values are characteristic of Anomalous behaviour/non fickian transport, suggesting that more than one mechanism may be involved in release kinetics. High the value of 'n' high is the polymer relaxation and swelling / erosion and drug is release in this fashion. For F2 the 'n' value is high shows that drug is released by high polymer relaxation and swelling / erosion.

The study also reveals that the process of preparation also affects the release patterns of the drug from the formulations of Oxprenolol Hydrochloride matrix tablets. Direct compression processes more suitable and hence the sustained release action is achieved.

Table No.1: Formulation of sustained release matrix tablets of Oxprenolol Hydrochloride using different polymer combinations

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Oxprenolol Hydrochloride	80	80	80	80	80	80	80	80	80	80	80	80
2	Oryza sativa	40	80	-	-	-	-	40	80	-	-	80	40
3	Carrageenan	-	-	40	80	-	-	80	40	40	80	-	-
4	Gum Arabic	-	-	-	-	40	80			80	40	40	80
5	Lactose	160	120	160	120	160	120	80	80	80	80	80	80
6	Magnesium stearate	10	10	10	10	10	10	10	10	10	10	10	10
7	Talc	10	10	10	10	10	10	10	10	10	10	10	10
8	Total weight (mg)	300	300	300	300	300	300	300	300	300	300	300	300

Table No.2: Preformulation studies

S.No	Property	Result
1	Organoleptic character	Colour : white Odour : Odourless Texture : amorphous powder;
2	Hygroscopicity	Hygroscopic.
3	Bulk density	0.65g / ml
4	Tapped density	0.12 g / ml
5	Carr's index	18.5%
6	Angle of repose	38.91 ± 0.41
7	Solubility	Freely soluble in water.

Table No.3: Physico chemical properties of all natural polymers

S.No	Physicochemical parameters	Gum Arabic	Carrageenan	Oryza sativa
1	Solubility	Soluble in cold water. practically insoluble in ethanol	Soluble in water, insoluble in organic solvents	Practically insoluble in cold ethanol (96%) and in cold water
2	pH	4.5-5.5	4.5	4.5
3	Loss on Drying	≥15%	≥12%	5.10%
4	Bulk density (g/cc)	0.6	0.60	0.547
5	Tapped density (g/cc)	0.86	0.702	0.657
6	Carr's Index	30.23	16.32	18.17
7	Hausner's ratio	1.43	1.17	1.20
8	Angle of repose	31.1^0	28.42^0	33.07^0
9	Ash value	≥4	≥15%	10
10	Acid insoluble ash value	≥1	≥0.5	4

Table No.4: Compression Parameters

S.No	Formulation code	Bulk density(gm/ml)	Tapped density(gm/ml)	Carr's index (%)	Hausner's ratio	Angle of repose
1	F1	0.458	0.514	10.89	1.22	25.49
2	F2	0.454	0.519	12.52	1.14	25.13
3	F3	0.433	0.504	14.08	1.16	27.00
4	F4	0.462	0.514	10.11	1.11	25.11
5	F5	0.468	0.504	9.52	1.07	27.18
6	F6	0.439	0.517	15.08	1.17	27.18
7	F7	0.439	0.531	17.32	1.20	27.34
8	F8	0.452	0.519	12.90	1.14	27.46
9	F9	0.461	0.527	12.52	1.14	28.18
10	F10	0.463	0.541	14.80	1.16	25.31
11	F11	0.475	0.517	8.12	1.08	26.48
12	F12	0.428	0.528	17.8	1.21	24.14

Table No.5: Evaluation Tests for Post Compression Parameters

S.No	Formulation Code	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)	Weight variation (%)	Drug content (%)
1	F1	4.1	3.83	0.68	259	98.22
2	F2	3.8	3.93	0.72	263	97.44
3	F3	4.0	3.78	0.66	237	98.55
4	F4	4.1	3.88	0.78	250	96.89
5	F5	3.8	3.52	0.73	232	99.11
6	F6	4.2	3.76	0.69	257	97.23
7	F7	4.2	3.98	0.71	270	97.58
8	F8	4.3	3.87	0.66	251	98.55
9	F9	4.1	3.93	0.68	261	98.28
10	F10	3.8	3.76	0.71	266	96.38
11	F11	4.2	3.61	0.62	286	97.68
12	F12	3.9	3.96	0.79	242	96.36

Table No.6: *Invitro* drug release data of all formulations

S.No	Time (hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
2	1	27.81	28.82	27.68	25.72	23.36	23.32	29.12	39.89	29.94	27.14	31.28	27.81
3	2	34.26	34.24	35.16	34.94	29.74	28.46	39.91	44.85	35.23	39.21	49.68	34.26
4	3	42.31	42.94	46.13	44.97	39.16	38.28	45.68	55.54	47.33	41.77	58.24	42.31
5	4	47.85	51.21	53.21	51.80	43.21	42.64	56.24	60.57	53.12	48.32	65.74	47.85
6	5	58.41	58.88	59.94	58.99	47.26	45.19	66.31	64.87	63.31	55.64	69.32	58.41
7	6	65.06	69.14	62.89	61.24	52.36	50.04	77.11	71.16	67.94	60.68	75.38	65.06
8	7	76.61	77.45	68.09	65.09	61.69	56.92	83.38	78.1	69.33	68.88	80.16	76.61
9	8	81.41	79.58	70.22	70.37	63.24	61.78	86.23	83.85	72.24	75.33	82.73	81.41
10	9	85.82	85.23	73.63	72.89	66.38	63.71	90.16	90.21	78.21	78.24	88.3	85.82
11	10	88.10	87.32	78.40	75.22	72.91	67.32	92.27	94.44	89.32	83.61	92.21	88.1
12	11	89.32	94.32	87.42	87.43	83.14	75.08	93.97	96.34	92.16	85.41	93.41	89.32
13	12	90.25	99.37	90.77	--	85.40	81.5	95.01	97.34	94.21	89.32	94.65	90.25

Table No.7: Stability studies of best formulation (F2)

S.No	Parameter	Initial	1st month	2nd month	3rd month
1	Appearance	White glossy	White glossy	White glossy	White glossy
2	Thickness(mm)	3.93±0.14	3.95±0.10	3.98±0.12	3.99±0.11
3	Hardness(kg/cm2)	3.8±0.23	3.7±0.54	3.4±0.12	3.3±0.23
4	Friability (%)	0.72±0.01	0.72±0.01	0.76±0.08	0.82±0.09
5	Drug content	97.44±1.34	97.04±0.04	96.02±0.13	95.12±0.10

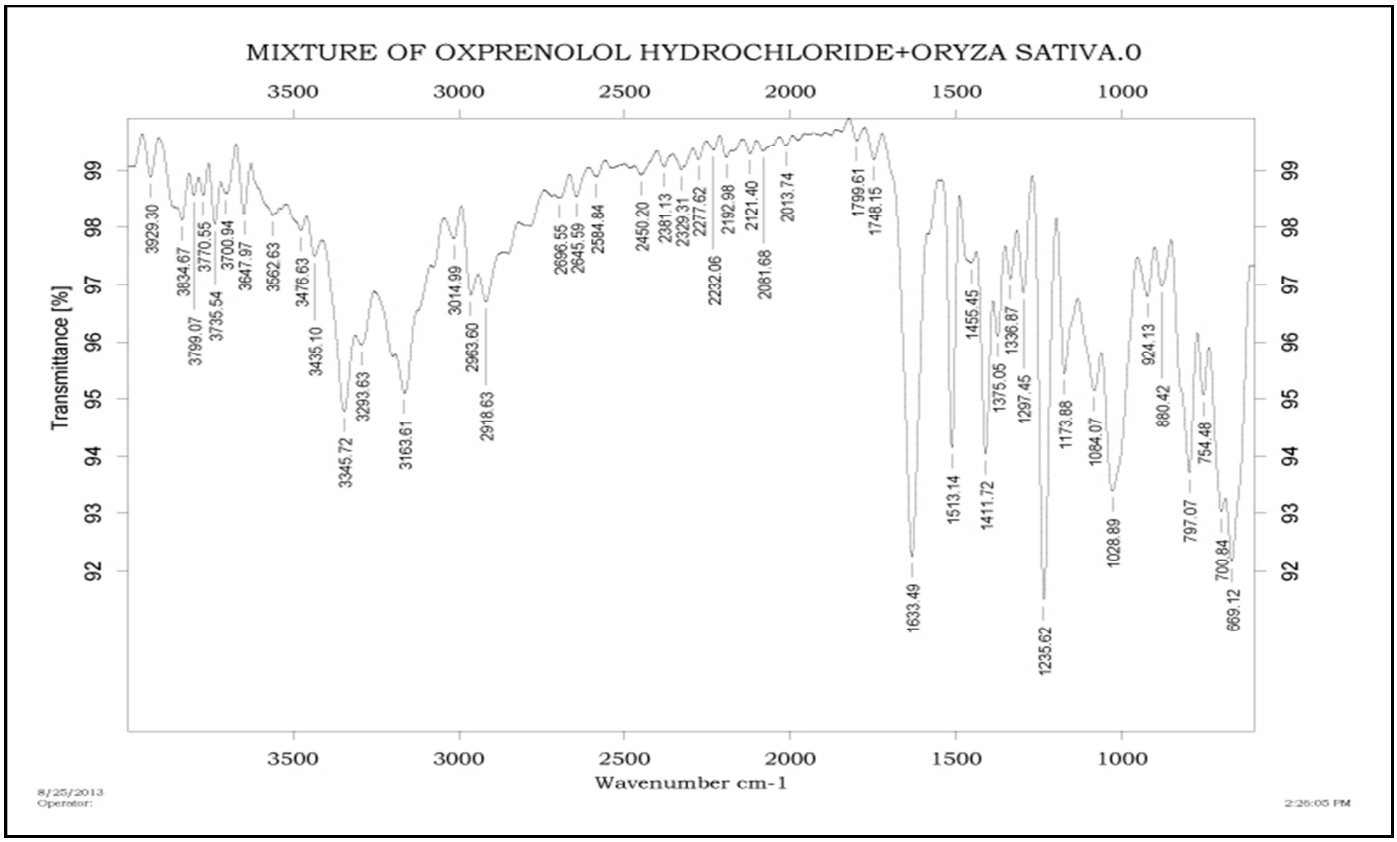

Figure No.1: FT-IR Spectrum of Oxprenolol Hydrochloride + Oryza sativa

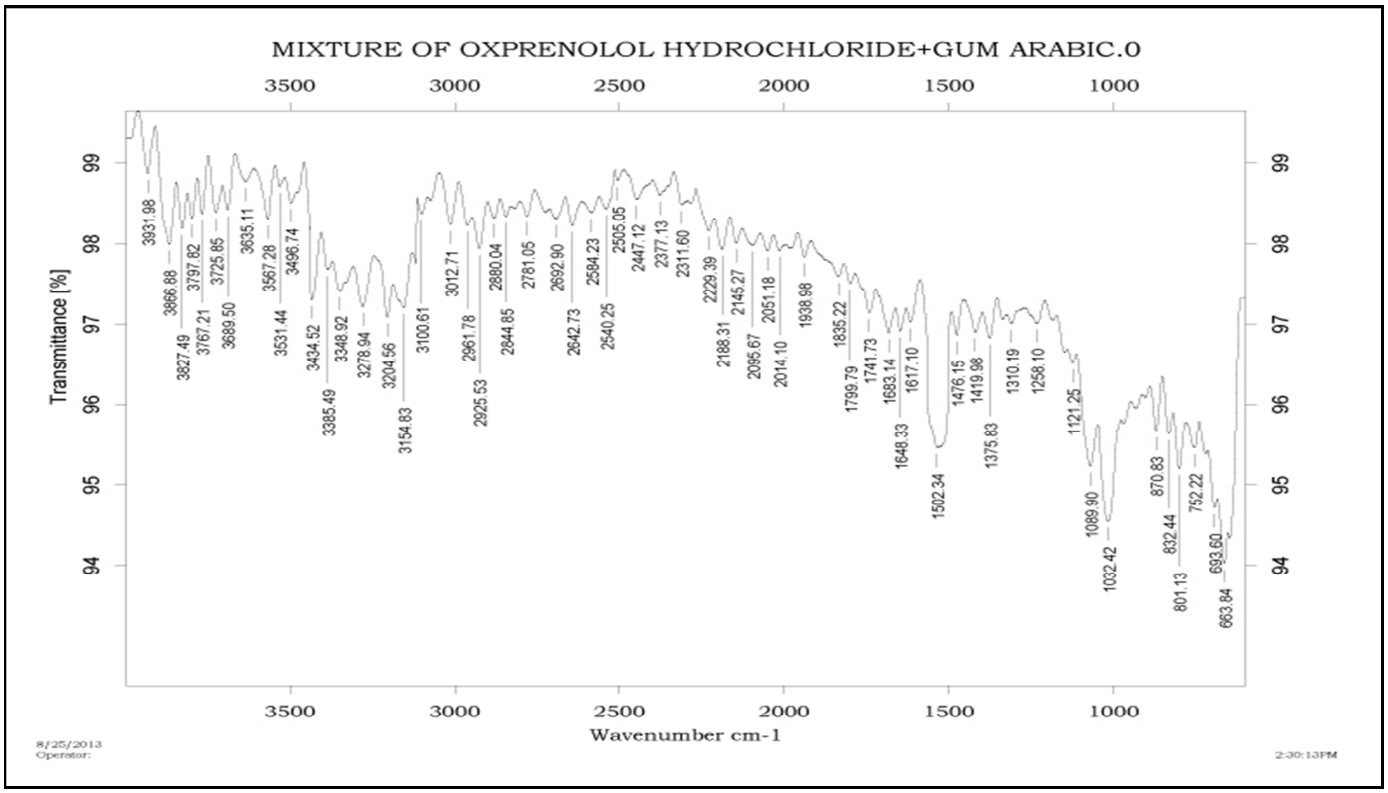

Figure No.2: FT-IR Spectrum of Oxprenolol Hydrochloride + Gum Arabic

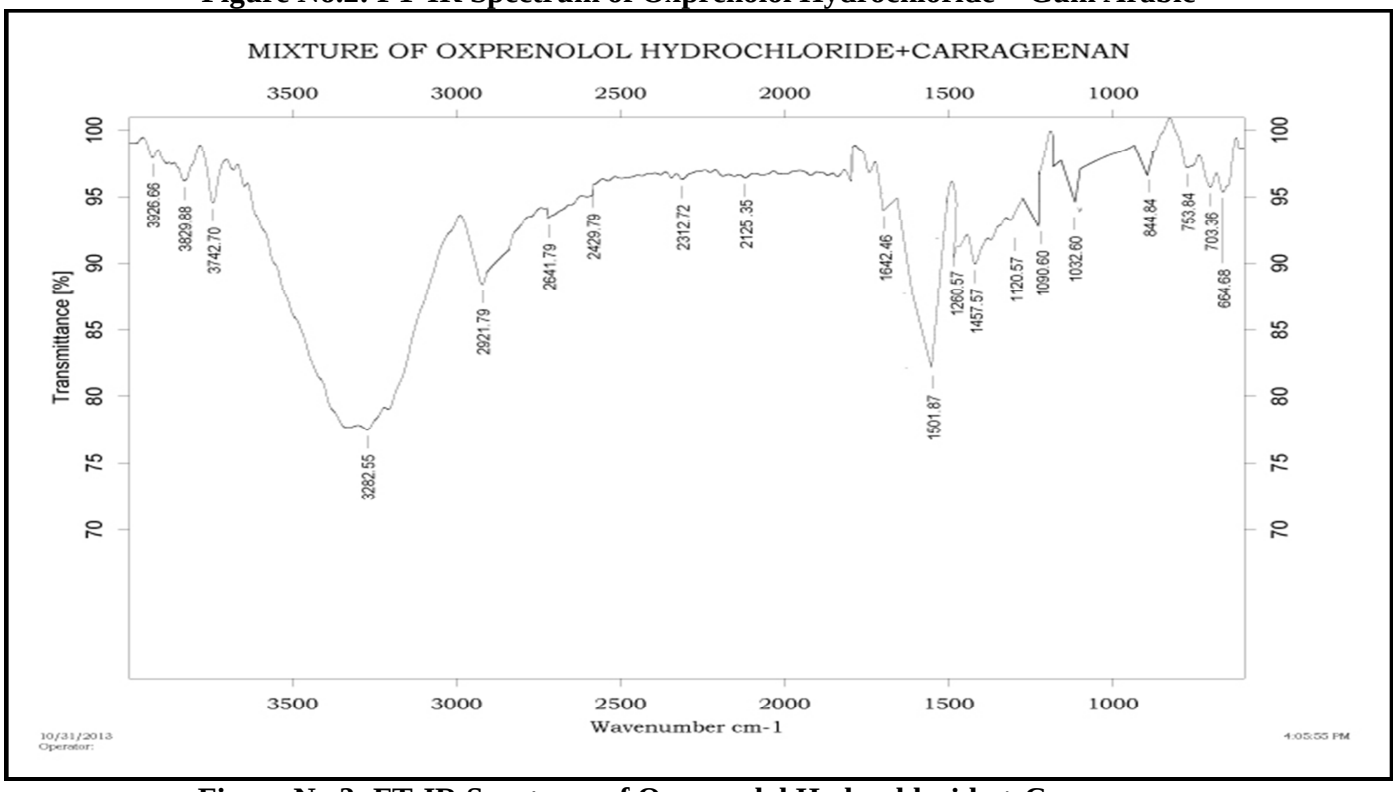

Figure No.3: FT-IR Spectrum of Oxprenolol Hydrochloride + Carrageenan

CONCLUSION

The polymer plays a major role in the design of sustained release matrix tablet.

The method of preparation of SR matrix tablets also plays the major role in the design of the sustained release matrix tablets.

The study reveals that the sustained release of Oxprenolol Hydrochloride is possible for choosing the Oryza sativa (natural polymer) as matrix former also shows anomalous diffusion.

Hence by the use of the Oryza sativa polymer as matrix once daily dose of Oxprenolol Hydrochloride (300mg) is achieved.

ACKNOWLEDGEMENT

Our college ASN COLLEGE OF PHARMACY, Tenali supports for doing this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Alekhya C H V. *et al*. A research article on formulation and evaluation of sustained release matrix tablets of Oxprenolol Hydrochloride, *International Journal of Research in Pharmaceutical and Nano Sciences*, 4(5), 2015, 290 - 297.