IJPSR (2011), Vol. 2, Issue 11 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 24 June, 2011; received in revised form 25 August, 2011; accepted 14 October, 2011

# DESIGN, DEVELOPMENT AND EVALUATION OF MATRIX TABLET CONTAINING INDIGENOUS MEDICINAL PLANTS

Trapti Rastogi* and Dr. S. S. Khadabadi

Government College of Pharmacy, Kathora Naka Road, Amravati-444604, Maharashtra, India

**Keywords:**
Matrix tablet,
Hydrophobic,
Polymer,
Dissolution,
*Boswellia serrata*,
*Moringa oleifera*

**Correspondence to Author:**

**Trapti Rastogi**

Research Executive, Simpex Pharma Pvt. Ltd., 1104-1107, 11th floor, Ansal Tower, Nehru Place, New Delhi-110019, India

## ABSTRACT

A Sustained release tablet formulation should ideally have a proper release profile that is usually encountered in manufacturing. The objective of the present investigation was to develop the sustained release matrix tablet of *Boswellia serrata, Moringa oleifera* and *Vitex negundo* using the combination of hydrophilic and hydrophobic polymers.Tablet formulations were developed using wet granulation method. Ethanolic extracts of *Boswellia serrata, Moringa oleifera* and *Vitex negundo* were used. Addition of different diluents like talc , magnesium stearate and microcrystalline cellulose were used for improving flow ability and compressibility. The tablets were subjected to physicochemical characterization, in vitro drug release and stability studies. The physicochemical properties were found within limits. The % drug release after 12 hours for formulation F-1, F-2, F-3 was found to be 97.32, 90.12, and 73.85 respectively. The presence of Ethyl cellulose as well as HPMC as the total matrix material significantly influenced the release rate of the drug. Based on dissolution studies all the formulations showed sustained release of drugs from the formulations.

**INTRODUCTION:** Inflammation and rheumatism remain serious problems in the present era. Inflammation is a key feature in autoimmune disease. Inflammation occurs as the immune system reacts to injury, infection, environmental agents, malignancy, and cellular changes. Any assault to living tissue, whether due to physical , chemical or microbiological origin results in inflammation, manifests by redness, heat, pain, swelling and loss of function.

A large proportion of the Indian population for their physical and psychological health needs depend on traditional, system of medicine. Medicinal plants have become the focus of intense study in term of conservation as to whether their traditional uses are supported by actual pharmacological effects or merely based on folklore.

The Indian traditional system of medicine especially ayurveda have put forward a number of therapeutic claims on plant drugs [1, 2, 3, 4, 5, 6, 7, 8, 9, 10].

Ayurvedic or homeopathic system of medicine claim that no side effects are generally observed on prolong use of herbal drugs.

Various formulations are available in the market of the plants *Boswellia serrata, Moringa oleifera* and *Vitex negundo* in the conventional dosage forms like tablet, capsule , ointment , gel etc. The available conventional formulations create various problems like fluctuation in drug blood level, patient's inconvenience, high dose potency etc. This problem can be solved by formulating sustained release matrix tablet using herbal drugs [2, 3, 29, 33, 34].

The anti-inflammatory activity of plants *Boswellia serrata, Moringa oleifera* and *Vitex negundo* is reported in the literature [6, 7, 10, 11, 12].

The successful treatment of inflammation depends on the maintenance of effective drug concentration level in the body for which a constant and uniform supply of drug is desired .

Sustained release dosage forms deliver the drug at a slow release rate over an extended period of time and achieve this objective. For sustained release system, the oral route of drug administration has by far received the most attention as complicated, convenient and safer route [13, 14].

Matrix tablets composed of drug and release retarding material offer the simplest approach in designing a sustained release system.

Hence in this study, an attempt was made to develop & evaluate safe and effective anti-inflammatory herbal matrix tablet containing *Boswellia serrata, Moringa oleifera* and *Vitex negundo* extracts by using combination of hydrophobic and hydrophilic polymers.

Currently available sustained release matrix tablets were generally prepared by wet granulation method.

**MATERIALS AND METHODS:** HPMC (K-4M, K-15M, K-100M), Ethyl cellulose were purchased from Loba Chem (Mumbai, India), Magnesium stearate, Microcrystalline cellulose and Talc were purchased from S.D. Fine Chem Limited, Mumbai, India. All other chemicals used were of analytical grade.

UV Visible spectrophotometer (Shimadzu UV 1700), Sonicator (Spectralab), Friability test apparatus (Roche friabilator), Dissolution test apparatus with auto sampler (V-Scientific DA-6D USP Standard), Compression machine (Rimek-Mini press) were the equipments used at various stages of this study.

**Plant material:** The gum resin of plant *Boswellia serrata,* the bark of plant *Moringa oleifera* and the leaves of plant *Vitex negundo* were collected from the local area of Amravati city. Dr. Prabha Y. Bhogaonkar, Director, Govt. Vidarbha Institute of Science and Humanities, Amravati, have done authentication. Voucher specimens and sample material was deposited in the Pharmacognosy & Phytochemistry Laboratory, Govt. College of Pharmacy, Amravati.

**Extract preparation:** The collected materials were washed thoroughly in water, chopped, air dried for a week at 35-40$^{o}$C and pulverized in electric grinder and exhaustively extracted successively in soxhlet apparatus,using petroleum ether, ethanol respectively.

The extracts were concentrated under reduced pressure.

**Preparation of tablets:** Number of studies shows the use of hydrophilic matrices to formulate the sustained release dosage forms of different drugs [15, 16].

A rapid rate of hydration of matrixing agent is necessary. A slow polymer hydration rate may be lead to dose dumping due to quick penetration of dissolution fluid in the tablet core. Hence a rapidly hydrating matrixing agent , HPMC K4M, HPMC K-15M, and HPMC-100M selected in the present study provide pH dependent drug release to oral dosage forms that can be used for formulating the sustained release dosage forms [17, 18, 19, 30].

However, the use of hydrophilic polymer alone for controlling the drug release of highly water soluble drugs is restricted due to rapid diffusion of the dissolved drug through the hydrophilic gel layer [18, 19].

Use of hydrophobic polymers will retard the drug release. So, in the present investigation, an attempt had been made to formulate the sustained release matrix tablets of the mentioned herbal drug combination using hydrophilic matrix material (HPMC K4M, HPMC K-15M, and HPMC- 100M) in combination with hydrophobic ethyl cellulose [35-40].

The compositions of the tablet formulations are given in **Table 1.**

The tablets were prepared by wet granulation technique as follow: [19, 20, 21, 22, 23]

The accurately weighed quantity of extract, polymer and other materials were passed through 60# sieve. Then mix drug and HPMC to obtain a uniform mixture.

This mixture is then granulated using weighed quantity of Ethyl Cellulose in iso- propyl alcohol and mix properly to obtain a dough.

The wet mass was passed through 8# sieve. Granules were dried in oven at 50±5°C for one hour and dried granules were passed through 20# sieve and were retained on 40# sieve , and 10% fines were added to these granules. Then these granules were lubricated in poly bag using talc and magnesium stearate. Weighed quantity of blend was fed to the hopper of compression machine. The granules compressed by using flat faced punch i.e., upper punch with break line and lower punch is plane of diameter 10 mm.

**TABLE 1: FORMULATION TABLE SHOWING COMPOSITION OF EACH MATRIX TABLET USING HYDROPHILIC AND HYDROPHOBIC POLYMERS**

| Formulation code.⇒ Ingredients (mg)⇓ | F1 | F2 | F3 |
|---|---|---|---|
| Extract of *Boswellia serrata* | 100 | 100 | 100 |
| Extract of *Moringa oleifera* | 100 | 100 | 100 |
| Extract of *Vitex negundo* | 100 | 100 | 100 |
| HPMC-K-M4 | 25 | - | - |
| HPMC-K-M15 | - | 25 | - |
| HPMC-K-100M | - | - | 25 |
| Ethyl Cellulose | 30 | 30 | 30 |
| Microcrystalline Cellulose | 37 | 37 | 37 |
| Magnesium Stearate | 4 | 4 | 4 |
| Talc | 4 | 4 | 4 |
| **Tablet weight (mg)** | 400 | 400 | 400 |

**Evaluation of granules** [20, 23, 26]**:** The granules containing above mentioned extracts prepared by wet granulatiuon method were evaluated for loose density, tapped bulk density, angle of repose and % compressibility index as mentioned in **Table 2.**

**TABLE 2: EVALUATION PARAMETERS OF GRANULES**

| Parameters → Formulations ↓ | Loose bulk density (LBD) | Tapped bulk density (TBD) | Carr's index (I) | Angle of Repose (Θ) | Total Porosity |
|---|---|---|---|---|---|
| **F1** | 0.424 ± 0.002 | 0.473 ±0.002 | 11.63 ±0.271 | 37.45±1.002 | 38.27 ±0.452 |
| **F2** | 0.306 ±0.015 | 0.355± 0.011 | 13.18 ±0.441 | 37.64 ±0.114 | 35.31 ±1.006 |
| **F3** | 0.316 ±0.048 | 0.356 ±0.036 | 11.31 ±0.097 | 35.91 ±0.50 | 35.05 ±0.646 |

**Physicochemical Characterization of Tablets** [20, 21]**:** The thickness and diameter of the tablets (n=3) were determined using vernier calipers. The hardness of the tablets (n=6) was determined by using Monsanto hardness tester. The (%) friability of the tablets (n=6) was determined using Roche friabilator. Weight variation test of the tablets (n=20) was carried out as per the official method (I.P. 1996). The results are shown in **Table 3.**

**TABLE 3: EVALUATION OF PHYSICAL PARAMETERS**

| Formulation Code | Thickness(mm) | Hardness (Kg/cm$^2$) | Friability (%) | Weight variation |
|---|---|---|---|---|
| **F1** | 3.51±0.049 | 4.68±1.140 | 0.18±0.008 | 409.4±0.003 |
| **F2** | 3.57±0.042 | 5.24±1.304 | 0.15±0.011 | 405.7±0.034 |
| **F3** | 3.62±0.041 | 5.82±0.836 | 0.16±0.007 | 407.5±0.049 |

***In- vitro* Dissolution Studies** [25, 26]**:** The in vitro release of total flavonoid from formulation batches was carried out in 0.1N HCl for 2 hours and continued in pH 6.8 phosphate buffer for remaining 10 hours. The studies were performed in USP dissolution apparatus II at 37±0.5 °C and 50 rpm. Samples were taken at interval of one hour each and analyzed for drug content at 415nm and replaced with same quantity of dissolution medium as it had withdrawn.

A dissolution study was carried out for each batch for 12 hours and drug release study was carried out on the basis of total flavonoid contents.

Since, flavonoid constitute are major chemical entity in formulation therefore we thought it logical to evaluate our formulation with respect to total flavonoid content.

Flavonoid content can be taken as the reliable and reproducible parameter for the dissolution studies of the formulation. So with respect to total flavonoid content present in extract, the drug release study was carried out.

The % drug releases of formulation batches containing HPMC and ethyl cellulose in 0.1N HCl for 2 hours and pH 6.8 phosphate buffer for remaining 10 hours are shown in **Table 4 and Fig. 1.**

**TABLE 4: PERCENT RELEASE PROFILES OF FORMULATIONS CONTAINING HPMC AND ETHYL CELLULOSE**

| Time (hrs.) | Percent Drug Release | | |
|---|---|---|---|
| | F1 | F2 | F3 |
| 1 | 38.89 | 37.68 | 34.59 |
| 2 | 48.49 | 46.65 | 42.47 |
| 3 | 55.52 | 51.93 | 47.78 |
| 4 | 60.41 | 54.91 | 52.53 |
| 5 | 65.89 | 56.46 | 54.81 |
| 6 | 69.19 | 60.45 | 57.78 |
| 7 | 73.23 | 65.61 | 59.91 |
| 8 | 77.62 | 72.32 | 60.42 |
| 9 | 80.41 | 78.86 | 62.11 |
| 10 | 87.68 | 83.04 | 64.46 |
| 11 | 95.82 | 87.24 | 70.70 |
| 12 | 97.32 | 90.12 | 73.85 |

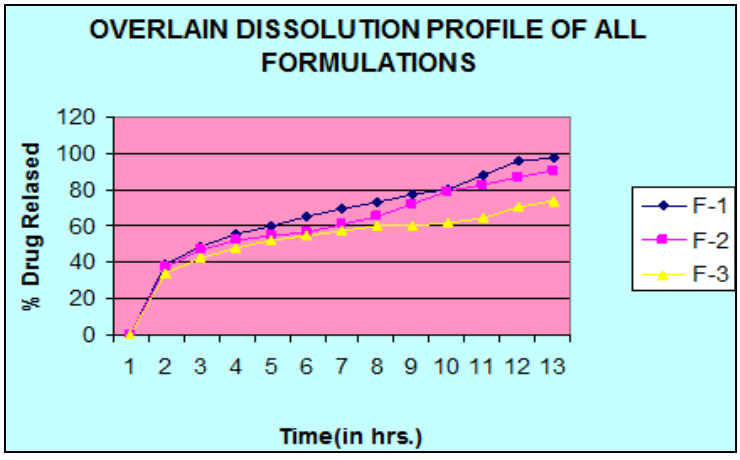


**FIG. 1: *IN VITRO* RELEASE PROFILE OF ALL FORMULATIONS SHOWING SUSTAINED EFFECT FOR TWELVE HOURS**

**Stability Studies** [27, 28]**:** Stability studies were carried out on the optimized formulations to determine the effect of various excipients on the stability of the drug based on ICH guidelines. Optimized formulations were kept for stability studies at 40 $^{o}$C and 75% RH for three months.

The release profiles of optimized formulations after stability studies for 3 months are shown in **Fig. 2.**

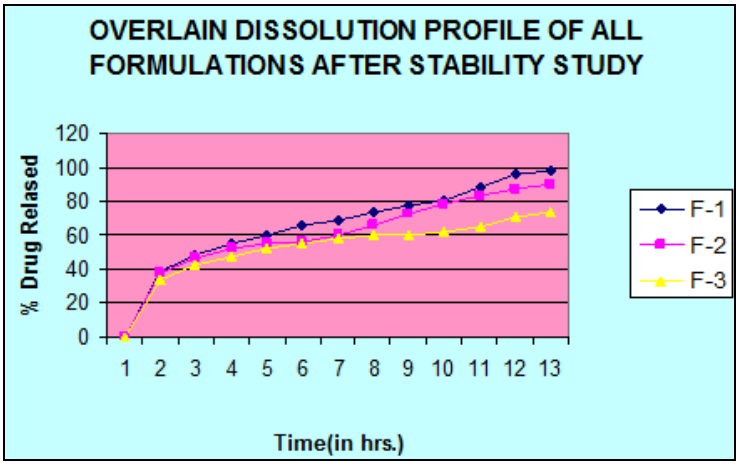


**FIG. 2: *IN VITRO* RELEASE PROFILE OF OPTIMIZED FORMULATIONS AFTER STABILITY STUDIES FOR 3 MONTHS**

**RESULTS AND DISCUSSION:** Herbal drugs now a days are receiving attention in finding the new source of promising drugs for the treatment and cure of various ailments.

The present research work is an attempt to design, develop and evaluate a stable Matrix Tablet of *Boswellia serrata*, *Moringa oleifera*, and *Vitex negundo*.

Sustained release matrix tablets of *Boswellia serrata, Moringa oleifera*, and *Vitex negundo* extract were prepared successfully using ethyl cellulose and hydroxyl propyl methyl cellulose as release retarding polymers by wet granulation method.

Evaluation parameters for the granules like bulk density, tap density, angle of repose, total porosity and Carr's index suggest that granules has good flow property.

Evaluation parameters for tablets like thickness, hardness, friability and disintegration of all formulations were found to be within pharmacopoeial limits.

The tablets passed the weight variation test as per I.P. The hardness of matrix tablets was found to be in the range of 4.68 to 5.82 Kg/cm$^2$.Friability values were found to be within acceptable limits. The friability values ranged from 0.15 to 0.18%.

From the results of physical evaluations, formulations were found to be stable and effective.

For the drug release in vitro dissolution studies had been performed as per method of USP. The in vitro release of total flavonoid was carried out for each batch for 12 hours.

Since, flavonoid constitutes are major chemical entity in formulation therefore we thought it logical to evaluate our formulation with respect to total flavonoid content. Flavonoid content can be taken as the reliable and reproducible parameter for the dissolution studies of the formulation. So with respect to total flavonoid content present in extract, the drug release study was carried out.

Table 4 and Fig. 1 shows the effect of different polymers on % drug release.

The % drug release after 12 hours for formulation F-1, F-2, F-3 was found to be 97.32, 90.12 and 73.85 respectively.

In the *in vitro* dissolution studies of matrix tablet Formulation F-1, containing HPMC-K4M along with Ethyl cellulose, it was observed that tablets were eroded and were able to form gelatinous layer around the tablet core and the drug release was found to be 69.19 % within 6 hours of dissolution study.

Drug release was decreased in Formulation F-2, containing HPMC-K15 M alongwith Ethylcellulose .The drug release was found to be 60.45% in the first 6 hours of the dissolution study.

In formulation F-3, containing HPMC-K100M along with Ethyl cellulose, drug release was found to be 57.78% in the first 6 hours of the dissolution study.

This release pattern may be due to a more rigid complex formed by hydrophilic polymer HPMC in presence of hydrophobic polymer Ethyl cellulose, which helped in retaining the drug in the matrix and did not allow rapid diffusion of soluble drug from the matrix.

The hydrophobic nature of Ethyl cellulose seems to have contributed towards reduction in the penetration of the solvent molecules into the matrix [32, 33, 34, 35, 36, 39].

As expected the release rate was slower with higher viscosities of HPMC. The molecular weight variations in HPMC are commonly expressed as viscosity grades. Larger viscosity grades correspond to greater polymer molecular weight.

Overall it can be concluded that, the presence of Ethyl cellulose as well as HPMC as the total matrix material significantly influenced the release rate of the drug.

Based on dissolution studies all the formulations showed sustained release of drugs from the formulations.

From results of stability studies, no significant change in *in vitro* dissolution profile and physical parameters was observed. Hence, the optimized formulations seem to be stable.

Based on above studies it can be concluded that developed matrix formulation can serve as a successful sustained drug delivery system.

**ACKNOWLEDGEMENT:** The authors are thankful to the Principal, Govt. college of Pharmacy, for providing necessary facilities to complete this research work.

**REFERENCES:**

1. Kirtikar, K.R.Basu, B.D. Indian Medicinal Plants, Periodical Book, New Delhi, II Edition,Vol III 1994: 1937
2. The Wealth of India, CSIR, New Delhi, 2003, Vol-X:SP-W: 522-523.
3. The Wealth of India, CSIR, New Delhi, 2003, Vol-II: B: 108.
4. The Wealth of India, CSIR, New Delhi, 2003, Vol-VI: M: 108.
5. S.G.Joshi, Indian Medicinal Plants, 2000,:400, 284, 109
6. Prajapati, Purohit, Sharma,Kumar, A Handbook of Medicinal Plants: pp:543
7. The Useful Plants of India, National Institute Of Science Communication,CSIR, 4th Edition. 682,380-381,78-79.
8. Kapoor L.D.,CRC, Handbook of Ayurvedic Medicinal Plants,CRC press,2001.pp:131-132.
9. C.P.Khare, Encyclopedia of Indian Medicinal Plants, Springer Berlin Heidelberg: 157-158.108-109,317-318.
10. Medicinal Plants of India, An Encyclopedia by Ravindra Sharma: 260.
11. The Ayurvedic Pharmacopoiea of India, Part-I, Vol-IV, First Edition, Government of India, Ministry of Health and Family

Welfare, Dept.of Ayurveda, Dept .of Ayush, New Delhi. 142-144.
12. The Ayurvedic Pharmacopoiea of India, Part-I, Vol-IV, First Edition, Government of India, Ministry of Health and Family Welfare, Dept.of Ayurveda, Dept .of Ayush, New Delhi. 50-51, 114-115.
13. Ansel H. C., Allen L. V., Ansel's Pharmaceutical Dosage forms and Drug Delivery Systems, 8th edition, 2005, Published by Lippincott Williams and Wilkins. 652-653.
14. Chien, Y. W., Canana, B. E. and Mares, S. E., In; Novel Drug Delivery System, 2nd edition, Marcel Dekker, Inc, New York, 1992. 1,301.
15. Robinson, J.R., *et.al*. Chapter 1."Influence of drug properties and route of drug administration on the design of sustained and controlled release systems" In Robinson, J.R., Lee, V.H.L., (Eds.), and Controlled Drug Delivery: Fundamentals and Applications, 2nd Edn, Vol. 3, Marcel Dekker, Inc., New York, 1978: 4.
16. Gupta, P. K., and Robinson, J.R, Chapter 6 ,Oral controlled Release SystemIn; Kydonieus, A., (Ed), Treatise on Controlled Drug Delivery, Marcel Dekker, 1992, 256.
17. Ansel, H. C., Popovich, N. G. and Allen, L. V., In; Pharmaceutical Dosage Forms and Drug Delivery Systems, 6th edition, B.I. Waverly Pvt. Ltd., New Delhi, 1999, 215.
18. Vyas, S. P. and Khar, R. K., In; Controlled Drug Delivery Concepts and Advances,1st edition, Vallabh Prakashan, Delhi, 2002, pp:7.
19. Hui ho-wah et al., Chapter 9. Design and Fabrication of Oral Controlled Release Drug delivery system In; Robinson, J.R., Lee, V.H.L., (Eds.), Controlled Drug Delivery: Fundamentals and Applications, 2nd Edn,Vol.-3, Marcel Dekker, Inc., New York, 1978, pp:373.
20. Lachman L, Lieberman H. A. and Kanig J. L., The Theory and Practice ofIndustrial Pharmacy, 3rd Edn, Varghese Publishing House, Bombay, 1990, 430.
21. Sarfaraj K. Niaji., Handbook of Pharmaceutical Manufacturing formulations, Compressed Solid Products, Vol-1, pp: 29.
22. James Swarbrick, James C. Boylan, Granulation, Encyclopedia of Pharmaceutical Technology, Vol-7:121-161.
23. K. Raghuram Reddy, Srinivas Mutalik, and Srinivas Reddy, Once-Daily Sustained-Release Matrix Tablet of Nicorandil: Formulation and *In Vitro* Evaluation, AAPS Pharm Sci Tech, 2003; 4 (4).
24. James Swarbrick, James C. Boylan, Controlled and Modified-Release Drug-Delivery System, Encyclopedia of Pharmaceutical Technology, Vol-3: 281.
25. James Swarbrick, James C. Boylan, Dissolution and Dissolution Testing, Encyclopedia of Pharmaceutical Technology, Vol-4: 121-169.
26. Shirwaikar, S. Jacob and V. Grover, Formulation and Evaluation ofSustained Release Tables Using An Insoluble Rosin Matrix System, Indian J. Pharm. Sci.., 2005, 67(1): 80-83.
27. ICH Q1A (R2), Stability Testing Guidelines: Stability Testing of New Drug Substances and Products: 1-22.
28. Stability of drugs and dosage forms by Sumie Yoshioka and Valentine J.Stellar:180.
29. Turner S.Federici, C.Hiti, M.London, C and Brunelle A, *In Vivo* and *In Vitro* Performance of a Novel Self Correcting 600mg 12 hour controlled Release formulation of Ibuprofen, SCOLR Pharma, INC.
30. Momin Munira, Pundarikakshudu K, Optimization and Pharmacotecnicalevaluation of compression coated colon-specific drug delivery system of Triphala using factorial design, Drug development research, 2005, Vol-65:34-42(27 ref.).
31. M.C. Gohl , D.Soni,.S.A. Nagori and K.G. Sarvaiya, Evaluation of Venlafaxine Hydrochloride Release from Press coated Matrix Tablet, Indian Journal of Pharmaceutical Sciences, May-June, 2008: 292-296.
32. S.Ganesh, M.Radhakrishnan, M.ravi, B.Prasannakumar and J.Kalyani , In vitro evaluation of the effect of combination of Hydrophobic and Hydrophilicpolymers on controlled release Zidovudine Matrix Tablets, Indian J.Pharm Sci.,July-Aug, 2008.
33. Munira Momin, K Pundarikakshudu , S.A. Nagori, Design and development of Mixed film of Pectin: Ethyl cellulose for colon specific Drug delivery of Sennosides and Triphala,Indian J.Pharm Sc., May-June 2008: 338-343.
34. K.M.Manjunatha, M.V.Ramana and D.Sattyanarayana,Design and evaluation of Diclofenac Sodium Controlled Drug Delivery Systens , Indian J.PharmSc., May-June,2007:384-388.
35. Rama Krishna, Raparla, T.E.G.K. Murthy, Formulation and Evaluation of Oral controlled release Glimepiride Matrix Tablets , Adv.Pharmcol. & Toxicol ,Vol -8(2),2007:59-62.
36. Kamla Pathak, Revi Shekhar, Reshu. Preparation and Evaluation of three layer matrix tablet for the oral controlled delivery of Tramadol Hydrochloride, The Pharma Review, (Dec.2007- Jan 2008).
37. Hosseinali Tabandeh, Seyed Alireza, Mortazavi , Tina Bassir Guilabni, Preparation of Sustained release matrix tabletsof Aspirin with Ethylcellulose, Eudragit RS 100 and Studying the release profiles and their sensitivity to tablet hardness, Iranian Journal of Pharmaceutical Research (2003):201-206.
38. S. C. Basak, B.M. Jayakumar Reddy, K.P. Lucas Mani. Formulation andrelease behavior of sustained release Ambroxol hydrochloride HPMCMatrix tablet.
39. Munira Momin and K.Pundarikakshudu. Design, Development and in-vitro evaluation of Sennosides Tablets containing Pectin HPMC for colonic DrugDelivery, Indian Journal of Pharm.Sci., May-June, 2007.

**********