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Formulation and Evaluation of Microcapsule of Lornoxicam by using non solvent addition method

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Abstract

Microencapsulation is processes through which very tiny droplets or particles of liquid or solid material are surrounded or coated with continuous film of polymeric Loroxicam were prepared by non solvent addition method employing n-hexane as non-solvent. Particle size usually ranges from 1-2000 micro meters. Lornoxicam is widely used non-steroidal anti-inflammatory agent. Lornoxicam has half life of 3-5 hours so it has to be taken frequently in day to achieve desired therapeutic concentration in plasma.

Key words: Polymer, Core Material, Anti-Inflammatory Agent, Continuous Film

Introduction

The aim of every drug delivery system is to make available a therapeutic amount of drug to correct site in body to attain quickly, & then maintain, desired concentration of drug. Drug delivery has two idealized objectives namely spatial placement & temporal delivery of drug. Spatial placement relate to targeting of a drug to a precise organ or tissue, while temporal delivery means to control the fate of drug delivery to target site. in spite of tremendous advancement in diverse drug delivery approaches, oral route remains the most acceptable route of drug administration because of low cost of therapy, ease of administration, & improved patient compliance.[1,2]

Microencapsulation is a process through which very tiny droplets or particles of liquid or solid material are surrounded or coated with continuous film of polymeric material.

- Microencapsulation may be as define as micro ionized drug particle or ultrafine drug droplets incorporated in capsule of some micro meter size.
- Particle size usually ranges from 1-2000 micro meters.
- Another terms- coated granules, pellets, seeds and microcapsule.
- Product smaller than 1 micro meter are referred to as “nanoparticles” when coating and core regions are not disintegrating then analogous form are used microparticles.

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- Walls may be single layer/multilayer.
- Microcapsules may contain one or more thousand of core substances[3]

Reasons behind Microencapsulation:

In some case core must be isolated from its surrounding as in isolating vitamin from deteriorating effect of oxygen.

- Retarding evaporation volatile core.
- Improving handling properties of sticky material.
- Control rate of which is leaves microcapsule and as in control release of drug.
- Taste and odor masking.
- Selective sorption.
- Reduced gastric irritation.
- Sustain release.
- Stabilization to oxidation.

Core Material

The core material, is specific material to be coated, it can be liquid or solid in nature. The composition of core material can be different as liquid core can include dispersed and/or dissolved material. The solid core can be a mixture of active pharmaceutical material, diluents, excipients, & stabilizers, release-rate retardants or accelerators. The capability to vary the core material composition provides flexibility & utilization of this characteristic often allows effective design & development of the preferred microcapsule properties. Liquid core may be polar or non polar in nature which may be active ingredient or that act as vehicles for dissolved or suspended drugs. Solvent properties of such liquid will influence rate of drug release and selection of coating material. Physiological acceptable buffer can be include in core containing

drug their release is less dependent on pH variation in different region of GI Solid cores used more frequently than liquid factor that can be considered in manufacturing[3]

Coating Material

Coating material should be able of forming a thin film that should be-:

- Cohesive with core material.
- Chemically compatible & non-reactive with core.
- Provide desire wetting properties like strength, flexibility, impermeability, optical properties and stability.
- Ability to release core material under specific condition that include pressure, temp, liquid permeability.
- Compatibility of erosions in certain conditions.
- Selection of coating material mainly depends upon nature of core material.
- If material are lipophilic then coating material hydrophilic polymer.
- Aqueous solution as core material water synthetic polymers.[3,4]

Method of Manufacturing:

In present work, Non solvent addition method was used to formulate microcapsule of lornoxicam. Non solvent addition method is come under Coacervation-Phase Separation method of microencapsulation.

Coacervation-Phase Separation:

This process consists of three steps -:

1. Formation of 3 immiscible chemical phases
2 Deposition of coating.
3. Rigidization of coating**.**

Step 1 a. The process includes formation of 3 immiscible chemical phase:1) a liquid manufacturing vehicle phase, 2)a core material phase & 3) a coating material phase.

b. To form three phase, core material is disperse in solution of coating polymers, solvent for polymer being liquid manufacturing vehicle phase.

c. The coating material phase, an immiscible polymer in a liquid state, is formed by using one of methods of phase separation-conservation, i.e., by changing temperature of polymer solution; or by adding a salt, non-solvent, or incompatible polymer solution.

Step 2 a. This process consists of depositing coating of liquid polymer upon core material. it, is done by control, physical mixing of coating material (while liquid) & core material in manufacturing vehicle.

b. Deposition of coating of liquid polymer around core material occurs if polymer is adsorbed at interface form between core material & liquid vehicle phase, & this adsorption phenomenon is a requirement to effective coating.

c. The continued deposition of coating material is promote by a decrease in total free, interfacial energy of system, decrease coating material surface area during coalescence of liquid polymer droplets.

Step 3 The process involves rigidizing coating, usually by thermal, cross-linking, or desolvation techniques, to produce self-sustaining microcapsule.

Non solvent addition method: In this method liquid which is non solvent for given polymer can be added to solution of polymer to induced phase separation resulting immiscible liquid polymer can be utilized to produce microencapsulation of an immiscible core material.

Table 3: Formulation Detail of Lornoxicam Microcapsules Using Synthetic Polymer

Ingredients	F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8	F 9
lornoxicam (mg)	10	10	10	10	10	10	10	10	10
Ethyl Cellulose (mg)	100	200	300	-	-	-	-	-	-
Eudragit RL 100 (mg)	-	-	-	100	200	300	-	-	-
Eudragit S 100 (mg)	-	-	-	-	-	-	100	200	300
Acetone (ml)	20	20	20	20	20	20	20	20	20
Heavy Liquid Parafin (ml)	60	60	60	60	60	60	60	60	60
n – Hexane (ml)	60	60	60	60	60	60	60	60	60
Tween 80 (ml)	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Speed (RPM)	900	900	900	900	900	900	900	900	900

Particle size and Shape study

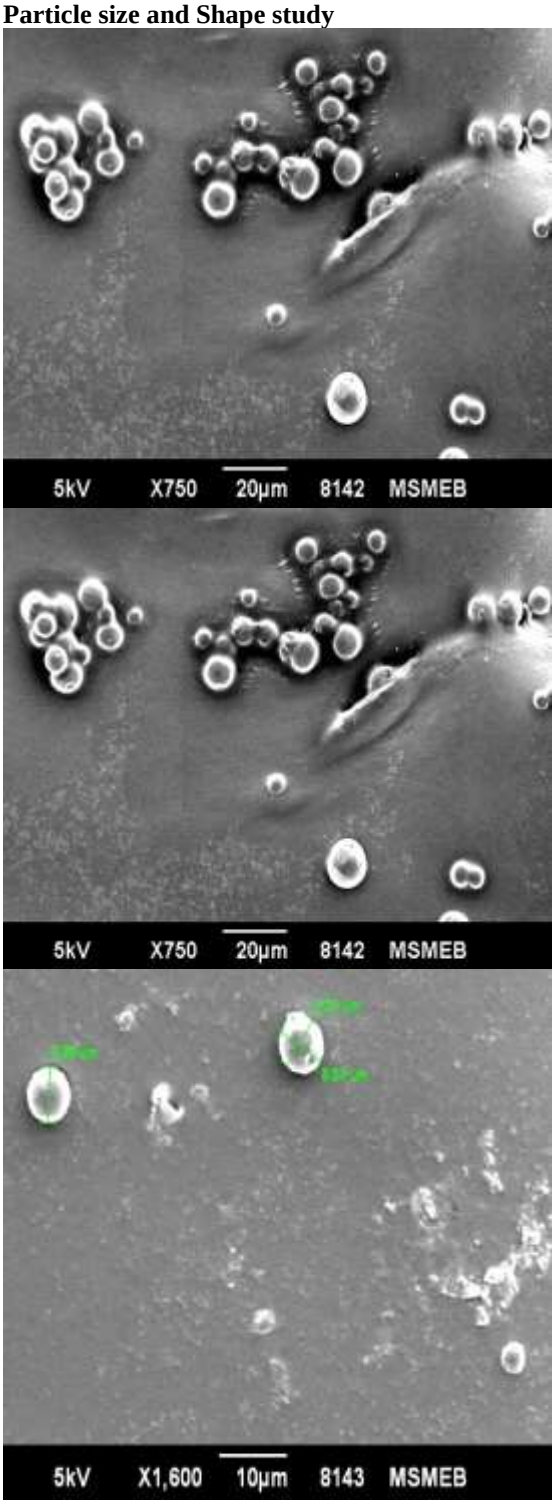

Fig. 1,2: SEM image of Formulation F3 using ethyl cellulose + lornoxicam

Percentage (%) yield: The yield of microsphere was determined by comparing the whole weight of microspheres formed against the combined weight of the copolymer & drug.

$$\text{Percentage yield} = \frac{\text{Mass of microspheres obtained}}{\text{Total Weight of drug and polymer used}} \times 100$$

Particle size and Shape: Particle size and particle size distribution of microcapsule were determined using the particle size analyzer.

Entrapment efficiency: Drug loaded microcapsule (10 mg) were powdered & suspended in 10 ml 0.1 N HCL solutions & kept for 24 hrs. It was stirred for 5 min and filtered by what man filter paper. For determination of entrapped drug, the amount of drug present in the clear supernatant after centrifugation was determined by UV spectrophotometer at 380 nm. A standard calibration curve is plotted for this purpose. The amount of drug in supernatant was then subtracted from the total amount of drug added during the preparation.The drug entrapment efficiency was calculated by the following equation

$$\% \text{ Entrapment Efficiency} = \frac{Pc}{Tc} \times 100$$

Where, Pc = Practical content
Tc = Theoretical content

Rheology Properties

Angle of repose, cars, index, bulk density, and hen's ratio were determined to assess the flow ability of the prepared microcapsules.

Determination of swelling properties:

The swelling property of microcapsules in the dissolution medium was determined. Microcapsules of known weight were kept in dissolution solution for 4 hrs. & swollen microcapsules were collected by a centrifuge & wet weight of swollen microcapsule was determined by first blotting particles with filter paper to remove absorbed solvent on surface & then weighing immediately on a electric balance. The percentage of swelling microcapsules in the dissolution media was then calculated by using equation.

$$Sw = \frac{(Wt - Wo)}{Wo} \times 100$$

Where, Sw = percentage of swelling of microcapsules
Wt = weight of microcapsule as time t
Wo = initial weight of microcapsule +Z

Determination of percentage of moisture loss:

The loaded microcapsules was evaluated for percentage of moisture loss which sharing an idea about its hydrophilic nature. The microcapsules weighed initially kept in desiccators containing calcium chloride at 37 c for 24 hours. The final weight was noted when no further changes in weight.

$$\% \text{ Moisture loss} = \frac{\text{Initial Weight} - \text{Final Weight}}{\text{Final Weight}} X100$$

In – Vitro release studies

In – vitro release studies were carried out using paddle type of apparatus at 37 ± 0.5º C in 900 ml of 0.1 N NaoH for 24 hrs. Microcapsule equivalent to 100 mg of product is kept in to apparatus & rotated to 50 rpm. A sample of 10 ml was withdrawn at various time intervals like 0, 2, 4, 6, 8, 10, 12 , 14 and 16 hrs& filtered, analyzed by UV spectrophotometrically at 380 nm .

Results and Discussion

Solubility studies

The sample was tested for its solubility in various solvents. Obtained results are shown in table

Table 4: Solubility Profile of Lornoxicam

Sr. No.	Medium	Solubility Profile
1	Water	Insoluble
2	Methanol	Vey slightly soluble
3	Ethanol	Very Slightly soluble
4	0.1 N hydrochloric Acid	Very Slightly Soluble
5	0.1 N Sodium Hydroxide	slightly Soluble
6	Acetone	Slightly Soluble
7	Acetonitril	Very Slightly Soluble
8	0.1 N NAOH	Slightly Soluble
9	Phosphate buffer pH7.4	Slightly Soluble

Melting Point

Table 5: Melting Point Range of Lornoxicam

Sr. No.	Onset	Complete	Melting Point
1	225°C	230º C	230 ± 2ºC
2	222º C	230º C	

Calibration Curve

lornoxicam solution was scanned in the U.V. range of 200-400 nm using The spectrophotometric method of analysis of lornoxicam at λ_{max} 380 nm was found to be reproducible and highly sensitive. The standard curves of lornoxicam were prepared in distilled water & 0.1N NaOH solution, at λ_{max} 380 nm. The data were regressed to obtain the straight line. The correlation coefficient greater than 0.99 was observed in all the cases, which indicated that, the drug follows Beer-Lambert's law in the concentration range of 2-10 µg/ml.

Table 6: Calibration Curve of lornoxicam in 0.1N NaOH at λ_{max} 380 nm

Sr. No.	Conc. (µg/ml)	0.1 N NaOH
1	2	0.069
2	4	0.136
3	6	0.208
4	8	0.279
5	10	0.362

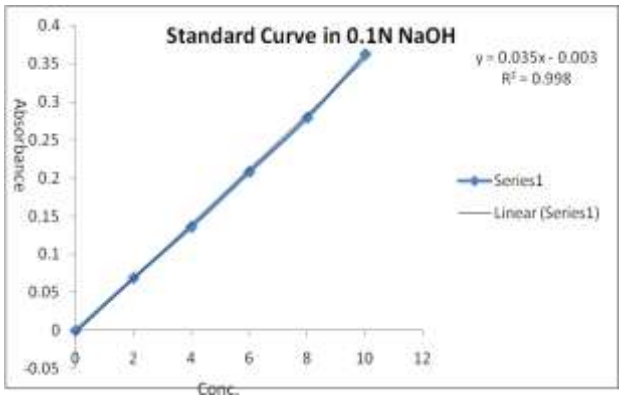

Fig. 3: Standard curve in 0.1N NaOH of lornoxicam

Fourier-Transform Infra Red spectroscopy (FTIR) Study:

The IR spectrum of drug substance was taken using IR spectroscopy. The presence of characteristic peaks associated with specific structural characteristics of the drug molecule was noted. Various peaks of the drug are shown in figure 4 its band frequencies.

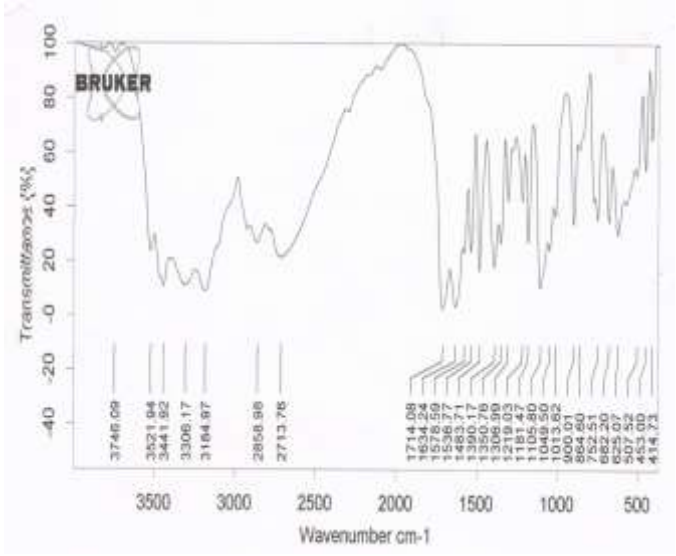

Fig. 4: FTIR of Lornoxicam

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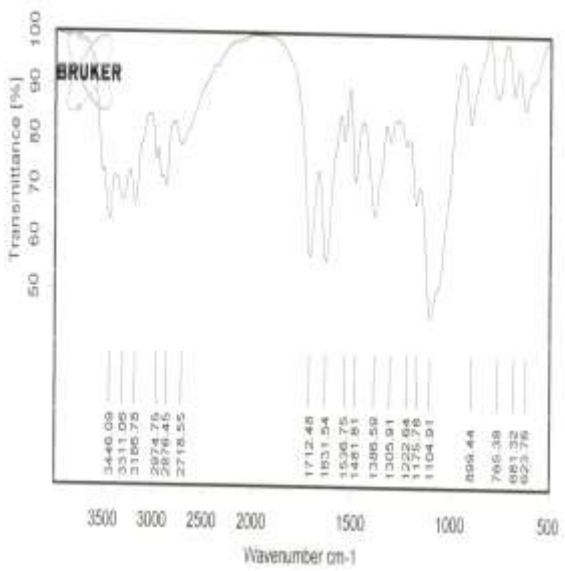

Fig. 5: FTIR of lornoxicam + Ethyl Cellulose

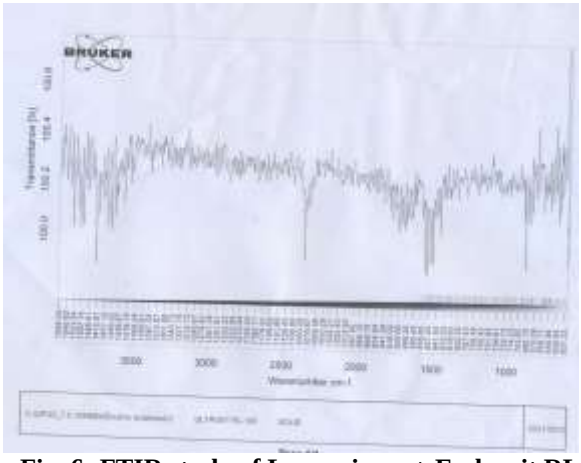

Fig. 6: FTIR study of Lornoxicam + Eudragit RL 100

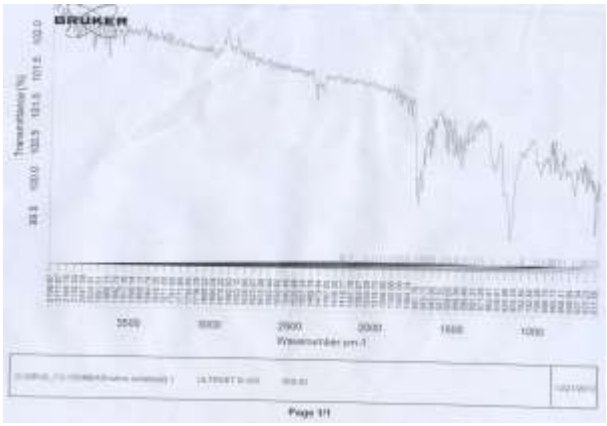

Fig. 7: FTIR of Lornoxicam + Eudragit S 100`

Percentage (%) yield & Encapsulation efficiency

Table 7: Percentage Yield, Drug Content of lornoxicam loaded microcapsule

Formulation	Yield (%)	Theoretical drug content (mg)	Practical Content (mg)	Encapsulation efficiency (%)
F1	63.32	30	22	51.69
F2	68	30	23.4	54.84
F3	62.65	30	24.8	64.53
F4	66.66	30	20	48.55
F5	65.66	30	22.7	53.45
F6	67	30	23.1	56.22
F7	66	30	20.8	53.01
F8	62.65	30	21.8	55.66
F9	64.66	30	22.4	59.18

Rheology Properties

Table 8: Various Rheology Properties of Microcapsule

Formulation	Carr's Index	Hausner Ratio	Angle of repose
F1	12.5	1.14	20.7
F2	9.82	1.09	23.6
F3	8.0	1.08	26.5
F4	4.5	1.04	20.4
F5	8.11	1.10	23.4
F6	6.66	1.07	22.4
F7	11.61	1.13	20.1
F8	13.15	1.15	21.4
F9	12.09	1.12	22.7

Swelling Properties

Table 9: Swelling Properties of microcapsule of lornoxicam

Formulation	Initial Weight (mg)	Final Weight (mg)	% Swelling
F1	50	89	78
F2	50	91	82
F3	50	99	98
F4	50	88	76
F5	50	92	84

F6	50	94	88
F7	50	85	70
F8	50	90	80
F9	50	95	90

Table 10: Moisture loss of microcapsule of lornoxicam

Formulation	Initial Weight (mg)	Final Weight (mg)	Moisture Loss	% Moisture Loss
F1	200	191.25	8.75	4.57
F2	200	189.25	10.75	5.68
F3	200	187.25	12.75	6.80
F4	200	189.28	10.72	5.66
F5	200	185.25	14.75	7.96
F5	200	181.50	18.50	10.19
F7	200	184.64	15.36	8.31
F8	200	180.75	19.25	10.65
F9	200	178.45	21.55	12.05

Drug Release Studies

Table 11: Drug release Kinetic of Formulation of lornoxicam microcapsules.

Sr No	Formulation	Drug Release
1	F1	76.89
2	F2	80.15
3	F3	83.45
4	F4	52.42
5	F5	60.01
6	F6	65.51
7	F7	75.02
8	F8	78.42
9	F9	79.96

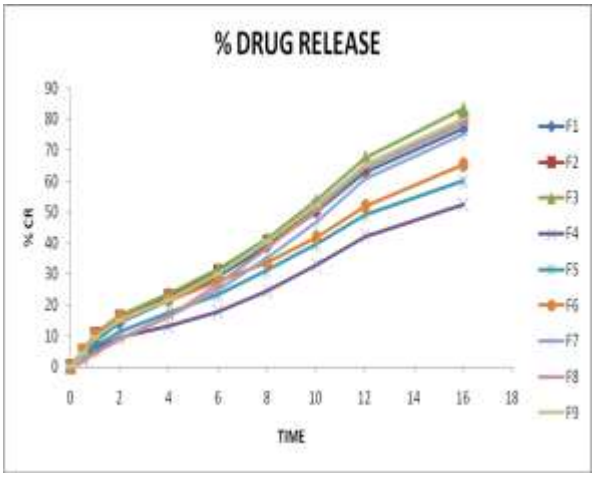

Fig. 8: Drug release studies in hours Drug Interaction Study

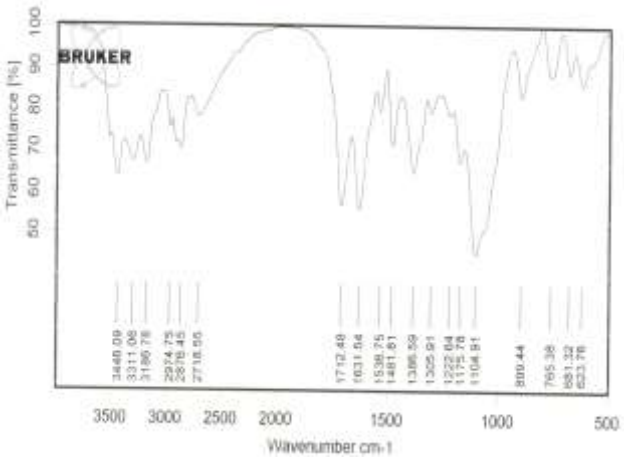

Fig. 9: FT IR study of formulation F3

Conclusion

Ethyl cellulose, Eudragit Rl 100 and Eudragit S 100 microcapsules containing Loroxicam were prepared by non solvent addition method employing n-hexane as non-solvent. The microcapsules were obtained in various size ranges & were found to be discrete, free flowing & spherical as evident from Scanning Electron microscopy study shown in fig 1,2. The sizes could be separated & a more uniform size of microcapsules could readily be obtained. Entrapments efficiency, drug content and % of yield results are shown in table 7 and also the rheological properties of microcapsule was shown in table 8. The Carr's index was acceptable range as per I.P. the swelling properties and the moisture loss were shown in table 9 and 10 respectively. The release from microcapsules was studied in 0.1 N NaOH for a period of 16 hours. Lornoxicam release from microcapsules was slow and spread over an extended period of time. The drug Release from microcapsules depends on the size of the microcapsules. Among all the formulation F3 found to be best formulation as its release profile is better then other, it may be due to correct ratio of drug and polymers. The use of particular manufacturing technique in the manufacturing of microcapsule depends on the nature of the polymer employed, nature of drug to be encapsulated, intended use of the system & intended duration of the therapy. The various parameter that can be externally controlled to yield micro particle of desired physicochemical characteristics, drug entrapment efficiency and drug release rate properties including the nature and solubility of the drug to be encapsulated, polymer type and concentration, its molecular weight, composition of the copolymers, drug loading concentration , type and volume of the organic solvent, the water phase

volume, pH, temperature, concentration, types of surfactant, and the mechanical speed of agitation.

References

1. D.M Brahmankar & Sunil B. Jaiswal, Biopharmaceutics & Pharmaceutics, Vallabh prakashan, New Delhi.335-354.
2. Drug bank:www.drugbank.ca
3. Mohanraj Palanisamy, Jasmina Khanam, Arun Kumar N and Rani C, Chitosan Microspheres Encapsulated With Metoprolol Succinate: Formulation and In Vitro Evaluation, Research J. Pharm. and Tech., 2009; 2(2): 349-352.
4. AY Pataquiva Mateus , MP Ferraz , FJ Monteiro, Nano-hydroxyapatite microspheres for periodontitis treatment: preparation and cytotoxicity studies Instituto de Engenharia Biomédica, Porto – Portugal, 2FEUP – Faculdade de Engenharia da Universidade do Porto, Departamento de Engenharia Metallurgic e de Materiais, Porto – Portugal.
5. Meixia Jin, Yanping Zheng, Qiaohong Hu, Preparation and characterization of bovine serum albumin alginate/chitosan microspheres for oral administration, Asian Journal of Pharmaceutical Sciences, 2009; 4(4): 215-220.
6. Vikas P., Dabber A.,Surya Parkas G., Neeraj Upmanyu, Neha Parashar, Vinod Mudgal, Formulation and evaluation of biodegradable microspheres of Tinidazol, International Journal of Drug Delivery,2010,238-241.
7. Kannan K, Karar PK, Manavalan R, Formulation and evaluation of sustained release microspheres of Acetazolamide by solvent evaporation technique, J. Pharm. Sci. & Res., 2009; 1(1): 36-39.
8. Chinna gangadhar B., Shyam sunder R., et al., Formulation and evaluation of Indomethacin microspheres using natural and synthetic polymers as controlled release dosage forms,International Journal of Drug Discovery, 2010;2(1):08-16.
9. Shen Hongliang, Wang Qiang, Qian Fang et al., Treatment of soft tissue wound with seawater by administration of livofloxacin chitosanmicrosphere at early stage, Medical Journal of Chinese People's liberation army, 2006;3.
10. Appa rao,study of prolong released microcapsules of Diclofinac sodium, International Journal of Drug Delivery ,2010;244-253.
11. Ravindra Reddy 2010,Development and characterization of mucoadhesive microcapsule,Indian journal of pharmaceutical,2010;11-25.
12. Bhabani S nayak,sustained release microencapsulated Drug delivery system ,2009;45-47.
13. Bipul nath 2009,desing of sustained relese floating microcapsules of Metformin HCL,2009;25-27.
14. Vikas Dash,Microencxapsulation of aspirin.2009,Microencapsulation of aspirin. International Journal of Drug Discovery,142-149
15. Sandile M.khamanga,Evaluate kinetics and mechanism of dru relese from microcapsule.2009;201-210.
16. Kannan K, Karar PK, Manavalan R, Formulation and evaluation of sustained release microspheres of Acetazolamide by solvent evaporation technique, J. Pharm. Sci. & Res., 2009; 1(1): 46-49.
17. Av yadav,Novel enteric microcapsule of Acelofenac,.journal of Indian pharmaceutical:34-45.
18. Md Abu Hena,study of indomethacin ,sustained relese microcapsule;2008,47-52.
19. Yoon 2004Study of Reseviour type microcapsules, 2004, , Medical Journal of Chinese People's liberation army, 2006;3
20. Flory, Paul J., Principles of Polymer Chemistry, Cornell University Press.
21. Reloar L R G: "The Physics of Rubber Elasticity, Oxford University Press", New York,1958.
22. Advances in Polymer Science, Vol. 109 & 110, Responsive Gels: I & II, Springer-Verlag.
23. Peppas N A: "Characterization of Cross-linked Structure of Hydrogels," Hydrogels Med.Pharm., 1, 27-56, 1986.
24. Brannon-Peppas L, "Preparation and Characterization of Cross-linked Hydrophilic Networks," Sud. Polym. Sci., 8, 45-66, 1990.
25. Hooper H H et al: "Swelling Equilibrium for Positively Ionized Poly(acrylamide) Hydrogels," Macromolecules, 23(4), 1096-1104, 1990.
26. Taylor, Bagley: "Tailoring Closely Packed Gel-Particles Systems for Use as Thickening Agents," J. Appl. Polym. Sci., 21, 113-122, 1977.

27. Taylor, Bagley: "Rheology of Dispersions of Swollen Gel Particles,"J. Polym. Sci.: Polymer Physics Edition, 13, 1133-1144, 1975.
28. Nae H N, Reichert W W: "Rheological Properties of Lightly Cross-linked Carboxy Copolymers in Aqueous Solutions," Rheologica Acta,31,(4), pp 351-360,1992.
29. Mohammad sadeghi1 and mojgan yarahmadi African journal of biotechnology vol. 10(57), pp. 12265-12275, 28 september, 2011
30. J. Kahovec, R. B. Fox and K. Hatada (2002). "Nomenclature of regular single-strand organic polymers". Pure and Applied Chemistry 74 (10): 1921–1956.
31. For example, in the online catalog of Scientific Polymer Products, Inc., poly(ethylene glycol) molecular weights run up to about 20,000, while those of poly(ethylene oxide) have six or seven digits.
32. French, Alister C.; Thompson, Amber L.; Davis, Benjamin G. (2009). "High Purity Discrete PEG Oligomer Crystals Allow Structural Insight". Angewandte Chemie International Edition48 (7): 1248–1252
33. Andersen, F. A. (1999). "Special Report: Reproductive and Developmental Toxicity of Ethylene Glycol and Its Ethers". International Journal of Toxicology 18 (3): 53–10
34. Anthony M. DiLauro, Alireza Abbaspourrad, David A. Weitz,and Scott T. Phillips. (2013) Stimuli-Responsive Core−Shell Microcapsules with Tunable Rates of Release by Using a Depolymerizable Poly(phthalaldehyde) Membrane American Chemical Society, 6, 3309−3313.

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