International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2422-2426 www.ijprajournal.com ISSN: 2456-4494

Formulation and Evaluation of Sustained Release Mucoadhesive Norfloxacin HCL Microparticles

Ram Mohan Trivedi, Mr. Santosh Shukla
Institute of Pharmaceutical Science and Research Unnao
Institute of Pharmaceutical Science and Research Unnao

Date of Submission: 20-06-2024 Date of Acceptance: 30-06-2024

ABSTRACT
In the present work, 6 different formulations were prepared by emulsificaion solvent evaporation method using three different polymers. They are Sodium Corboxy Methyl Cellulose(1:1 and 1:2), Sodium Alginate(1:1 and 1:2) and HPMC K100M (1:1 and 1:2).
Characterization of the drug was done by performing the UV spectroscopy and IR spectroscopy. IR spectrum of the pure drug was compared with that of physical mixture of drug with all the excipients used in the study. The results showed that there was no drug- excipient interaction.
All the prepared formulations were evaluated for Bulk density, Entrapment efficiency, drug content uniformity, Mucoadhesive strength, drug-polymer interaction, in-vitro drug release, Scanning electron microscopy, HPLC and short term stability studies.
The dissolution studies were carried out for 12 hrs. As per the result of dissolution study formulations(Table:9) F1(1:1), F2(1:2), F3(1:1) and F4(1:2) showed reasonable release 97.05, 95.151, 94.38 and 91.37 %, respectively. F1 and F2 showed good drug release profile, when compare to other formulations. Based on all these results, formulations F1 was selected as the best formulation.

I. INTRODUCTION

The concept of the advanced drug delivery systems especially those offering a sustained and controlled action of drug to desired area of effect, attained great appeal for nearly half a century. However, prior to advent of improved alternate methods, drug delivery systems were considered only as a means of getting the drug in to the patient's body. The actual practice of controlled release began with advent of timed-release coating to the pills or solid drug particles in order to mask their unacceptable taste or make them more palatable.

In the mid 1940 - 1960s, the concept of chemical microencapsulation technology began as an alternative means of delivering drugs. In continued quest for the more refined systems, in 1980s polymer membrane technology came to be known at forefront. Further, the process of targeting and site specific delivery with absolute accuracy can be achieved by attaching bioactive molecule to liposomes, bio-erodible polymer, implants, monoclonal antibodies and various particulate carriers (e.g., nanoparticles and microspheres, etc.). The micro-particulate delivery systems are considered and accepted as a reliable means to deliver the drug to the target site with specificity, if modified and to maintain the desired concentration at the site of interest without untoward effect(s).

Microspheres

A well-designed controlled drug delivery system can overcome some of the problems of conventional therapy and enhance the therapeutic efficacy of a given drug. To obtain maximum therapeutic efficacy, it becomes necessary to deliver the drug to the target tissue in optimal amount at the right period of time thereby causing little toxic and minimal side effect. There are various approaches in delivering a therapeutic substance to the site in a sustained controlled release fashion. One such approach is using microspheres as carrier for drug

Emulsification Solvent Evaporation Method for Preparation of Mucoadhesive microspheres:

Mucoadhesive microspheres were prepared by the w/o emulsification by solvent evaporation technique. The drug was dissolved in each polymeric aqueous solutions. The solutions were poured into 200 ml of sesame oil containing span-20 (0.5%) as an emulsifying agent. The aqueous phase was emulsified into the oily phase by stirring the system in 500 ml beaker at 500 rpm by mechanical stirrer. The beaker and its contents were heated on the hot plate at 80˚C. Continues stirring and heating were maintained for 4 hrs until the aqueous phase was completely removed by

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2422-2426 www.ijprajournal.com ISSN: 2456-4494

evaporation. The light mineral oil was decanted and collected microspheres were washed three times with 100 ml aliquots of n- hexane, filtered through what man filter paper, dried in an oven at 50˚ C for 2 hrs and stored in a dessicator at room temperature. Microspheres were prepared using Sodium Alginate, Sodium Carboxyl Methyl Cellulose and HPMC polymers.

Composition of Mucoadhesive Microspheres of Norfloxacin HCl:

Sl. No	Formulations	Drug (mg)	Sodium CMC (mg)	Sodium Alginate (mg)	HPMC (mg)	Drug Ratio
1	F1	500	500	-----	-----	1:1
2	F2	500	1000	-----	-----	1:2
3	F3	500	-----	500	-----	1:1
4	F4	500	-----	1000	-----	1:2
5	F5	500	-----	-----	500	1:1
6	F6	500	-----	-----	1000	1:2

Evaluation of microspheres

Bulk density (D_b):

It is the ratio of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of spheres was carefully poured into graduated measuring cylinder through large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in gm/cc and is given by,

$D_b = M / V_o$ Where, D_b = Bulk density (gm/cc)
M =Mass of powder (g)
V_o = Bulk volume of powder (cc)
Bulk density (gm/cm^3) = weight of sample / Final volume

Particle Size Analysis:

A minute quantity of microsphere was spread on a clean glass slide. This was placed in stage of calibrated optical microscope; approximately 100 microspheres were counted. The particle size was calculated in triplicate for each batch using the formula

Drug content:

Norfloxacin content in the microspheres was estimated by a UV Spectrophotometric method based on the measurement of absorbance at 272 nm in distilled water. Microspheres equivalent to 50 mg were weighed and added in 100 ml of distilled water. The volumetric flask was stirred continuously for 24 hrs on a magnetic stirrer. Dilutions of the above solutions were made suitably and measured for the drug content.

Drug Loading and Entrapment Efficiency:

Norfloxacin microspheres were weighed and dissolved in 0.N HCl. The UV absorbance of the solution was measured using a (Shimadzu UV-100 serious, Japan) 272 nm. Drug loading and encapsulation efficiency were determined by following formula and the values were expressed as percentage.

$$\text{Drug Loading} = \frac{\text{weight of Ciprofloxacin}}{\text{weight microspheres}} \times 100$$

In-vitro wash-off test for mucoadhesion:

The mucoadhesive properties of the microspheres were evaluated by in vitro wash-off test. A 1-cm by 1-cm piece of rat stomach mucosa was tied onto a glass slide (3-inch by 1-inch) using thread. Microspheres were spread onto the wet, rinsed, tissue specimen and the prepared slide was hung onto one of the groves of a USP tablet disintegrating test apparatus. The disintegrating test apparatus was operated such that the tissue specimen was given regular up and down movements in a beaker containing the simulated gastric fluid (pH 1.2). At hourly intervals at 37˚C, up to 3.5 hrs, the number of microspheres still adhering onto the tissue was counted. Percent mucoadhesion was given by the following formula.

% mucoadhesion = (no. of microspheres remains / no. of applied microspheres) ×100

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2422-2426 www.ijprajournal.com ISSN: 2456-4494

In-vitro drug release study:
Procedure:

In-vitro drug release studies of Norfloxacin HCl were conducted for a period of 12 hrs using USP XXIII type II apparatus at 37 ± 0.5^0 C and at 50 rpm speed in 900 ml of 0.1 N HCl (pH1.2). An aliquot of the sample was periodically with drawn at suitable time interval and volumes were replaced with fresh dissolution medium in order to maintain the sink condition. After withdrawing at predetermined time interval for 12 hrs, the samples were analyzed by a UV spectrophotometer (ElicoLI 120, Mumbai, India) at 272 nm. The study was performed in triplicate.

Evaluation parameters:
Particle size, Bulk Density, Drug content, Entrapment efficiency and mucoadhesive strenth:

Formulation	Particle Size (µm)	Bulk Density (gm/cm)	Drug content (%)	Entrapment Efficiency (%)	Muco Adhesive Strenth(%)
F1	97.21±0.57	0.271±0.21	82.56±0.34	72.72±0.13	64.11±015
F2	102.67±0.13	0.521±0.13	86.2±0.29	68.25±0.15	62.17±0.20
F3	74.75±0.12	0.47±0.17	83.15±0.88	67.71±0.21	58.14±0.19
F4	82.13±0.21	0.574±0.13	85.32±0.41	52.32±0.81	48.72±0.23
F5	68.83±0.32	0.596±0.12	76.51±0.27	58.21±0.21	46.26±0.72
F6	56.63±0.24	0.672±0.19	79.72±0.21	49.32±0.89	38.12±0.25

Correlation coefficients of different mathematical models for formulations F- 1

Formulation	Zero order $_R2$	First order $_R2$	Higuchi $_R2$	Peppa's	
				$_R2$	n value
F1	0.894	0.916	0.993	0.986	0.49

Stability Study:
Stability study data for F1

Sr. No.	Days	% R.D.C. 5-8^{O}C	% R.D.C. 27 ± 2^{O}C	% R.D.C. 40 ± 2^{O}C
1	0	100.00 ± 0.00	100.00 ± 0.00	100.00 ± 0.00
2	15	99.97 ± 0.024	99.95 ± 0.018	99.94 ± 0.034
3	30	99.84 ± 0.032	99.81 ± 0.026	99.73 ± 0.041
4	45	99.63 ± 0.045	99.54 ± 0.031	98.44 ± 0.037
5	60	99.24 ± 0.038	98.93 ± 0.021	98.80 ± 0.026

*Average of three readings
R.D.C. = Remaining Drug Content # = R.D.C. In pH 1.2 (0.1N HCl)

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 2422-2426 www.ijprajournal.com ISSN: 2456-4494

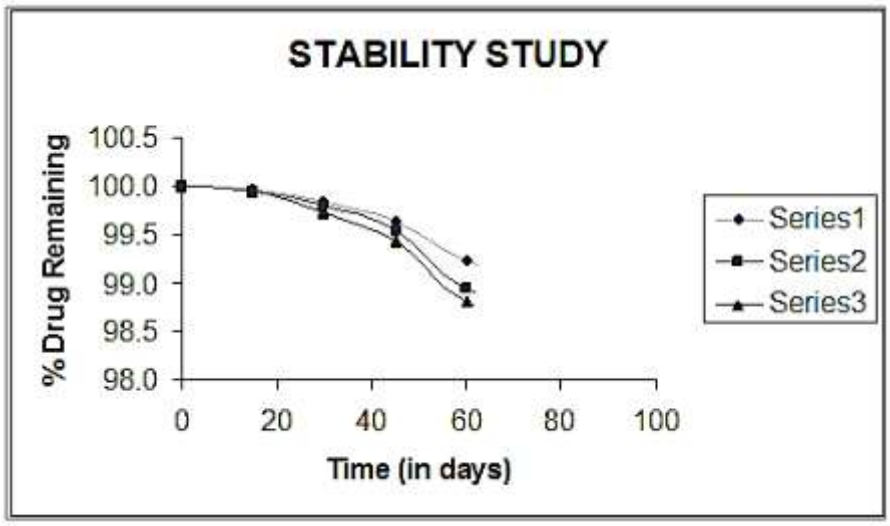

Fig 18: Stability study

Stability study is the important part of the study for any pharmaceutical formulation. There are procedures given for the stability study in ICH guidelines. In response to that stability study was carried out for the formulation F1(1:1) by exposing it to temperature 5-8^{o} C, 27^{o} C and 40^{0} C for 2 months. The sample was analyzed for drug content at regular interval of two months and it was evident that there was no remarkable change in the drug content of microparticles. Results show that formulation F1 was stable at mentioned temperatures. As the drug used, Norfloxacin HCl, is recommended to be stored below 25^{0} C, stability study has not been performed above ambient temperature.

REFERENCES

[1]. Suja C Jayan , Sandeep AV, Mohammed Rifash, Design and In-vitro Evaluation of Gelatin Microspheres of Salbutamol Sulphate, Hygeia 2009, 1,17.

[2]. Malay K. Das and Divya P Maurya, Evaluation Of Diltiazem Hydrochloride-Loaded Mucoadhesive Microspheres Prepared by Emulsification-Internal Gelatin Technique Acta Poloniae Pharmaceutica-Drug Research , 2008, .2,249-2598.

[3]. Parasuram Rajam Radhika, Moidutty Luqman, Chetan Hardas Borkhatria, Preparation and evaluation of delayed release aceclofenac microspheres. Asian Journal of Pharmaceutics- October-December, 16- 2008.

[4]. Patrick .B.O Donnell, James W.Mcginity, Preparation of microspheres by Solvent Evaporation technique, Advanced Drug Delivery Reviews 28(1997) 25-42.

[5]. D.Nagasamy venkatesh, Ajay Kumar Reddy, M K Samanta, B Suresh, Development and in vitro evaluation of colonic drug delivery system for Tagaserod Maleate, Asian Journal of Pharmaceutics-January-March 2009

[6]. Deepti Jain, Amulya K. Panda and Deepak K.Manjumdar, Eudragit S 100 Entrapped insulin microspheres for oral Delivery, AAPS Pharmascitech 2005; 6(1) Article 16.

[7]. Rajendra Kotadiya, Vishnu Patel, Harsha Patel, Hemangi Surti, Effect of hydrocolloid on the physicochemical Properties of Theophylline-loaded agar Microspheres Asian Journal of Pharmaceutics-April-June 2009.

[8]. Rassoul Dinarvand, Shadi H.Moghadam, Leyla Mohammadyari-Fard and Fatemeh Atyabi,Preparation of Biodegradable microspheres and Matrix Devices containing Naltrexone, AAPS pharm Sic Tech 2003;4(3) Article 34.

[9]. Raymond C Rowe, Paul J Sheskey and Sian C Owen, Handbook of Pharmaceutical Excipients, pg.369-376, 1474-1487.

[10]. Woodley J. Bioadhsion: New possibilities for drug administration, Clin.Pharmacokinet.2001; 40:77-84

[11]. Russsel G.F.Pharma.Int.4, 260, 1983

[12]. S.Tamizharasi, J.C.Rathi and V.Rathi, Formulation and evaluation of pentoxifylline-loaded poly (ε-caprolactone) microspheres, Indian Journal of pharmaceutical science May-June 2008, 333-337.

[13]. Santanu Ghosh and B.B.Barik, preparation and evaluation of Aceclofenac sustained release formulation and comparison of formulated and marketed products; IJMMS; 1 (9); 375-382; 2009.