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FLURBIPROFEN MICROSPHERES FOR THE TREATMENT OF ARTHRITIS

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ABSTRACT

Oral modified-release multiple-unit dosage forms have always been more effective therapeutic alternative to conventional or immediate release single-unit dosage forms. Novel drug delivery systems have several advantages over conventional multi dose therapy. Recent trends indicate that micro particulate drug delivery systems are especially suitable for achieving controlled or delayed release oral formulations with low risk of dose dumping, flexibility of blending to attain different release patterns as well as reproducible and short gastric residence time. Microspheres received much attention not only for prolonged release, but also for targeting of drugs. Micro particulate drug delivery systems provide tremendous opportunities for designing new controlled and delayed release oral formulations, thus extending the frontier of future pharmaceutical development. In future, microspheres will find the central place in novel drug delivery, particularly in diseased cell sorting, diagnostics, genetic materials, targeted and effective drug delivery. The current aim of this research paper is to study various aspects of the micro particulate drug delivery system including method of formulation, evaluation and characterization.

KEYWORDS: Microspheres, Controlled release, Novel Drug Delivery.

MATERIALS AND METHODS

Introduction

Microspheres based drug delivery system has received considerable attention in recent years. Microspheres of biodegradable and non biodegradable polymers have been investigated for sustained or controlled release depending upon the final application. The most important characteristic of microspheres is the microphase separation methodology which endows it

with a controlled variability in degradation rate and also drug release.[1] "Monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles" can be defined as structure made up of continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level. Microspheres are small spherical particles, with diameters in the micrometer range (typically 1μm to 1000 μm). Microspheres are sometimes starches, gums, proteins, fats and waxes. Arthritis means joint inflammation, but the term is used to describe around 200 conditions that affect joints, the tissues that surround the joint and other connective tissue. It is a rheumatic condition.

Fast facts on arthritis

- Arthritis refers to around 200 rheumatic diseases and conditions that affect joints, including lupus and rheumatoid arthritis.
- It can cause a range of symptoms and impair a person's ability to perform everyday tasks.
- Physical activity has a positive effect on arthritis and can improve pain, function, and mental health.[2]

MATERIALS

Flurbiprofen, Sodium alginate, calcium chloride, Magnesium stearate, Liquid Paraffin, Wax, Hexane, Isopropyl Alcohol. All the chemicals were of analytical grade.[3]

METHODS

Preparation of microspheres by modified emulsification method

The microspheres were prepared by using modified emulsification.[4] The drug Flurbiprofen [(1%) 0.5gm] was dispersed in aqueous solution of sodium alginate (2.5-7.5 g) with magnesium stearate (0-2 g). The solution was then emulsified in liquid paraffin containing span 80 using a mechanical stirrer at 1700 rpm for 1 h. After this, calcium chloride (2.5-5.0 g) solution (in isopropyl alcohol) was added to the emulsion at the rate of 2 ml/min. The emulsion was stirred for 10 more min. Microspheres formed in organic phase were removed by filtration and washed with hexane to remove liquid paraffin. Microspheres were then vacuum dried for 48 h. The composition of different batches is shown in Table 1.

Table 1: Formulation of different batches.

Batch code	Amount of Sodium Alginate(g)X_1	Amount of $CaCl_2$(g) X_2	Amount of Magnesium Stearate (g)X_3	Drug (mg)
F1	2.5	2.5	0	1
F2	2.5	2.5	2	1
F3	3.0	2.5	0	1
F4	3.0	2.5	2	1
F5	3.5	2.5	0	1
F6	3.5	2.5	2	1

RESULTS

Preformulation studies

❖ **Organoleptic properties**[5]

Flurbiprofen was tested for organoleptic properties such as

- Appearance-Powder
- Color-White
- Odor-odorless
- Taste-Bitter
- Melting point 117^0C
- Solubility- the solubility of Flurbiprofen was found to be very less as 0.0249 mg/ml in water.

According to the test results, it is clear that drug procured from Roha plant Maharashtra is giving satisfactory results and can be considered as good quality pure drug.[6]

Evaluation of microspheres

❖ **Particle size analysis**:- Particle Size Analysis was carried out by using particle size analyzer (Shimadzu). About microspheres suspension was taken selected and their size was determined by using optical microscope fitted with standard micrometer scales.

A- Without magnesium stearate

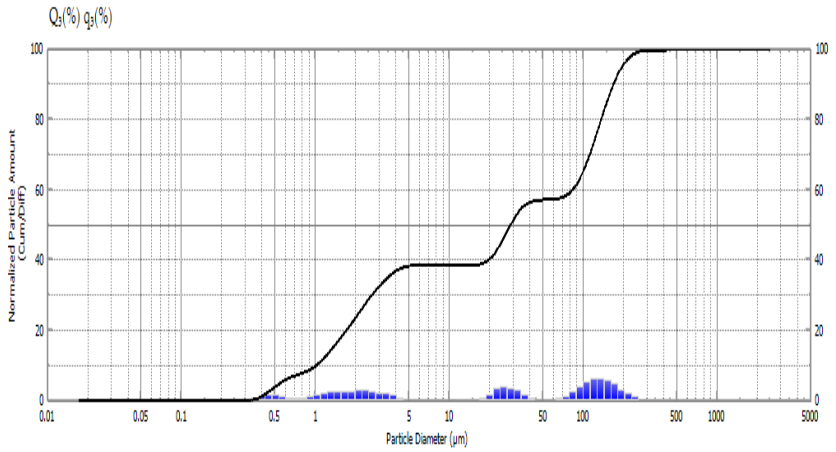

Fig. 1: PSA range in this graph 200±0.005 µm.

- 0.5 µm to 400 µm but maximum frequency was found around 200±0.005 µm
- **X-Axis** = Particle size µm, **Y- Axis**= Particle size quantity (%)

B- With magnesium stearate

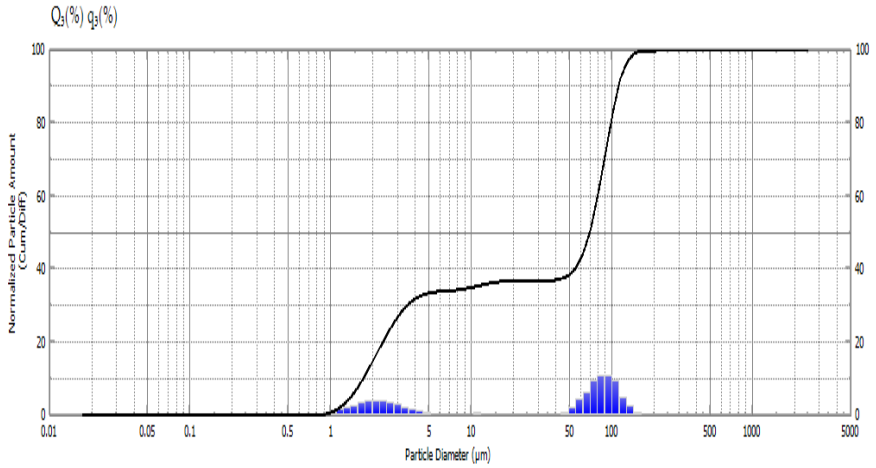

Fig. 2: PSA range in this graph 200±0.005 µm.

- 0.5 µm to 400 µm but maximum frequency was found around 200±0.005 µm
- **X-Axis** = Particle size µm, **Y- Axis**= Particle size quantity (%)

In-vitro drug release studies

The study was done for 20 hours with an optimum interval of sampling. From the study of release, pattern showed F1 showed a better release others with percentage cumulative drug release of 58.0±0.5.

Table 2: Percentage drug release from microspheres of formulation F1 to F6.

Hours	F1	F2	F3	F4	F5	F6
0.5	1.72±0.6	1.79±0.4	1.83±0.6	1.98±0.1	2.11±0.2	2.35±0.3
1	3.45±0.3	3.88±0.3	3.66±0.6	3.92±0.4	4.22±0.7	4.7±0.5
2	5.98±0.7	7.16±0.5	9.22±0.2	8.42±0.3	10.34±0.5	9.4±0.2
4	12.2±0.1	14.32±0.6	14.64±0.7	16.01±0.6	16.88±0.5	18.8±0.6
6	22.4±0.3	21.48±0.1	24.54±0.3	23.82±0.7	23.57±0.8	28.2±0.5
8	27.6±0.6	28.64±0.2	29.28±0.8	33.48±0.5	34.38±0.6	32.6±0.7
10	35.73±0.4	35.8±0.6	38.57±0.9	40.05±0.7	45.86±0.4	47.0±0.4
12	42.18±0.2	46.96±0.5	45.87±0.7	47.84±0.2	53.46±0.3	56.45±0.1
14	47.9±0.6	50.12±0.7	51.24±0.4	56.93±0.4	56.91±0.6	62.31±0.3
16	52.2±0.8	57.28±0.3	61.79±0.6	64.03±0.8	65.39±0.7	74.23±0.8
18	55.8±0.4	64.44±0.5	65.29±0.4	71.87±0.7	74.1±0.4	82.38±0.5
20	58.0±0.5	71.6±0.3	73.98±0.6	77.1±0.4	84.36±0.8	86±0.1

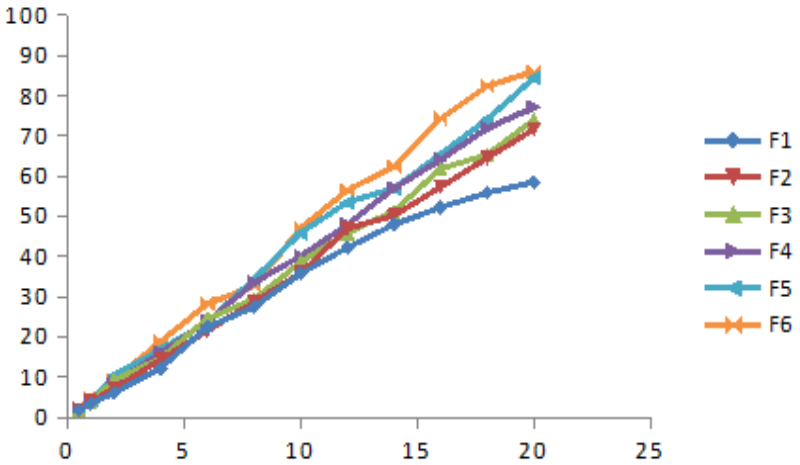

Fig. 3: *In vitro* drug release study of formulation F1-F6.

DISCUSSION

Flurbiprofen loaded sodium microspheres were prepared by using emulsification technique. Sodium alginates, a natural polymer which get degraded in acidic environment, non toxic. Optimal formulation of sodium alginate microspheres were selected by results like % entrapment efficiency, size of microspheres, shape, and % drug release from all six formulations. The concentration of sodium alginate had significant impact on drug entrapment efficiency and particle size.[7]

Microspheres of all batches had faster initial drug release. However, the drug release was more at higher concentration of sodium alginate as the concentration increases from F1 to F6. Sodium alginate polymeric solution was too viscous to pass through needle therefore

microspheres could not formed at higher concentrations. As the concentration increases from F1 to F6 (sodium alginate 2.5 – 3.5mg), initial drug release increases. After initial burst release, the release was slow and sustained, depending upon the polymer: drug ratio. After 20 hours, it was found to increase from 58.0±0.5 % for F1 to 86±0.1% for F6. (**Figure 3**). The formulation F1 showed better sustained release at the end of the 20th hour as compared to other batches. This may be due to better loading, encapsulation efficiency and increased particle size as compared to other batches.

CONCLUSION

The microspheres of Flurbiprofen prepared by emulsification method using natural polymer sodium alginate were able to sustain the drug release efficacy. The evaluation parameters like entrapment efficiency and in vitro drug release studies were done for the microspheres and found to be satisfactory. Microspheres prepared with 2.5% sodium alginate with and without magnesium strearate where found to be most appropriate sustained release formulation at the end of 20hrs.

The result of the study revealed that the use of natural polymer sodium alginate is an effective strategy for the designing and development of flurbiprofen microspheres. It was found to be easy, reproducible and effective sustained release drug delivery for the treatment of Arthritis, which can be further tested in animals and human beings in future as an effective treatment for Arthritic inflammation.

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