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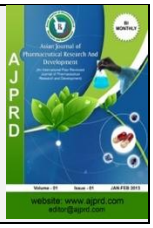

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Research Article

Fabrication of Nanogel for Topical Drug Delivery of Montelukast

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ABSTRACT

A novel nanocrystal system of montelukast (MTK) was designed to improve the transdermal delivery, while ensuring chemical stability of the labile compound. MTK nanocrystal Nanogel was fabricated using using nano dispersion method (Modified emulsification diffusion method). In the pre-formulation study, there was not any physicochemical interaction between drug and polymer had been evaluated by FTIR. The melting point was found to be 134- 137 0C. It is freely soluble in Cyclohexane & butanol ratio and water. The standard curve of ondansetron had been prepared by Cycloheaxxane & butanol (7:3). Montelukast nanogel were prepared by nanodispersion method. Formulations of different drug ratio were optimized with selected parameters like particle size, PDI, Zeta potential, entrapment efficiency, clarity test. pH test of gel, viscosity and gelation temperature. Drug release studies were performed by dialysis bag diffusion technique at a temperature (37°C). The study was continued for 24 hours till. The maximum amount of drug montelukast release 87% within 24 hr. The study was monitored at 37°C. Preparation, characterization and drug release study of montelukast loaded nanogel. This approach of montelukast loaded nanogel with chitosan as the polymer is quite successfully developed.

Keywords: Montelukast; Nanogel; Transdermal delivery; Topical Drug Delivery

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INTRODUCTION

Nanotechnology is bridge the barrier of biological and physical sciences which shows bridge by applying nanostructures and nanophases at various fields of science; specially in nanomedicine and nano based drug delivery systems, where such particles are of major interest. Nanomaterials can be well-defined as a material with sizes ranged between 1 and 100 nm, which influences the frontiers of nanomedicine starting from biosensors, microfluidics, drug delivery, and microarray tests to tissue engineering. Nanotechnology employs curative agents at the nanoscale level to develop nanomedicines.

NANOGEL

The term 'nanogels' defined as the nanosized particles formed by physically or chemically crosslinked polymer networks that is swell in a good solvent. The term nanogel was first introduced to define cross-linked bifunctional networks of a polyion and a nonionic polymer for delivery of polynucleotides (cross-linked polyethyleneimine (PEI) and poly (ethylene glycol) (PEG) or PEG-cl-PEI)[1]. Sudden outbreak in the field of nanotechnology have introduced the need for developing nanogel systems which proven their potential to deliver drugs in controlled, sustained and targetable manner. With the emerging field of polymer sciences it has now become inevitable to prepare smart nano-systems which can prove effective for treatment as well as clinical trials progress[2-8].

Nanogels are superior drug delivery system than others because

1. The particle size and surface properties can be manipulated to avoid rapid clearance by Phagocytic cells, allowing both passive and active drug targeting.
2. Controlled and sustained drug release at the target site, improving the therapeutic efficacy and reducing side effects. Drug loading is relatively high and may be achieved without chemical reactions; this is an important factor for preserving the drug activity.

3. Ability to reach the smallest capillary vessels, due to their tiny volume, and to penetrate the tissues either through the paracellular or the transcellular pathways[10].
4. Highly biocompatible and biodegradable. A model of drug release from nanogel is given in figure.

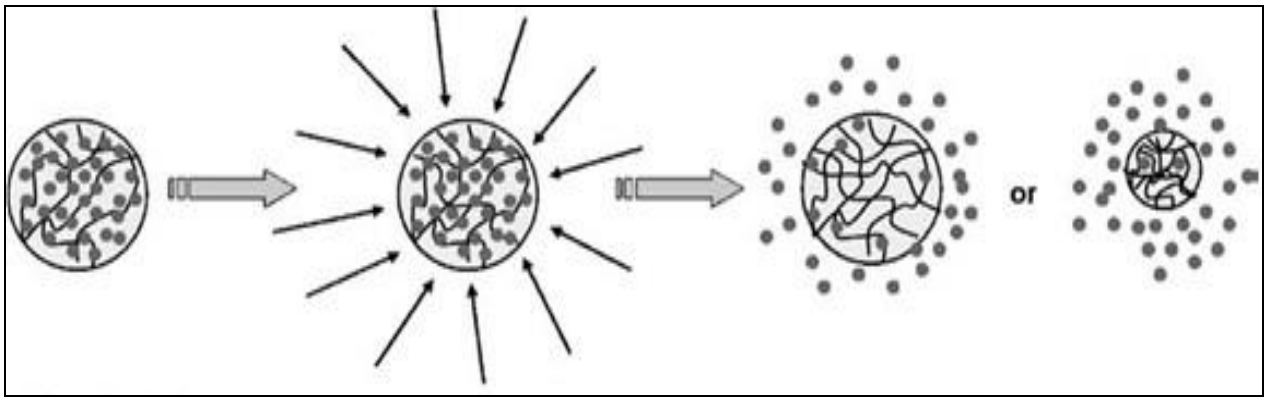

Figure 1- Drug release model from nanogel

METHODS OF PREPARATION OF MONTELUKAST SODIUM NANOGEL

Nanogel were prepare by using nano dispersion method (Modified emulsification diffusion method)

- Montelukast sodium was weighed 5 mg and dissolved in solvent containing polymer. This organic phase containing drug polymer mixture was added into the aqueous phase containing Tween 80, with constant stirring at 5,000-10,000 rpm using.
- Addition of organic phase was done with the help of syringe positioned with needle directly into the aqueous stabilizer solution at the rate of 0.5 ml/min.
- The resulting dispersion was stirred for 6 min at 10,000-25,000 rpm and was subjected to the sonication for 5- 10 min.
- Then double distilled water was added slowly to the dispersion with subsequent stirring for 1 hour to induce diffusion of organic solvent into the continuous phase and leading to the formation of nanodispersion.
- Organic solvent- Cycloheaxane & Butanol (7:3)[11-15]

Optimization of Formulation

Optimization of drug loading efficiency of Montelukast sodium x in Nanogel. Here in the table showing the various formulation schemes and processing variables on the basis of drug-polymer ratio.The different formulation show in table no1.[16-18]

Table: 1 Formulation code of different Drug-polymer-solvent ratio.

INGREDIENTS	F1	F2	F3	F4	F5
Montelukast sodium	5	10	15	20	25
Chitosan	100	100	100	100	100
Kappa Carragean	10	10	10	10	10
Cyclo heaxane & butanol (as solvent)	10	10	10	10	10

RESULTS AND DISCUSSION

Particle Size Analysis and Poly Disparity Index

The mean partial size was determined by dynamic light scattering (DLS) method using Horiba Scientific nanoparticle size analyzer. Size analysis was done in the aqueous state so because of hydration Z value is considered. All data represented in the form of mean diameter ± standard deviation. PDI is the unit less quantity and it represents the polydispersity of the formulation.

Table 2: Particle Size Analysis of Formulation

Formulation code	Average particle size(nm)	PDI
F1	113.6±7.2	0.402±0.032
F2	206.9±9.6	0.503±0.058
F3	327.2±11.3	0.419±0.023
F4	649.3±15.2	0.426±0.049
F5	739.0±15.6	0.485±0.051

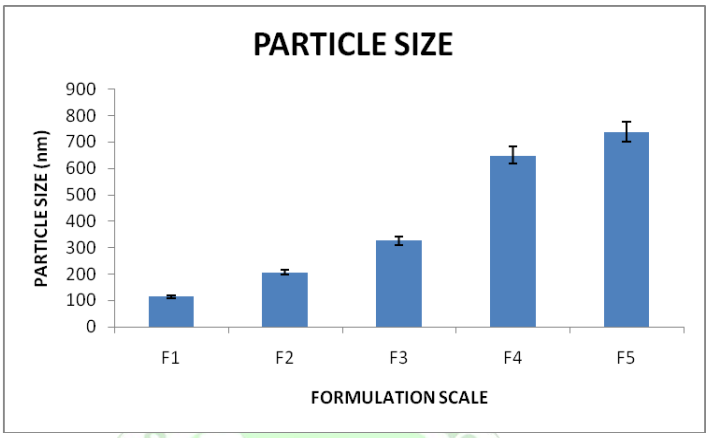

Figure 2: Paricle Size Graph of Nanogel

From the study, it was observed that drug-polymer ratio have a significant effect on particle size. The range of particle size is 113.6 to 739.0 nm. And the range of PDI is 0.402 to 0.485. Increased Drug concentration yields the larger nanogel. An adequate size and low PDI, which shows the acceptable monodispersity in the formulation, had to be considered as the choice for the final nanogel synthesis.

Zeta Potential

Zeta potential was determined by Horiba Scientific nanoparticle size analyzer for different formulations. Value of the zeta potential gives the idea of the potential stability of the colloidal solution. High values of negative or positive charge repel each other and indicate good stability. Magnitudes of zeta potential are tabulated in Table 3.

Table 3: Zeta Potential of different formulation

Formulation code	Zeta potential (mV)
F1	37.3±1.5
F2	39.6±1.2
F3	40.7±1.1
F4	78.9±0.8
F5	83.9±0.5

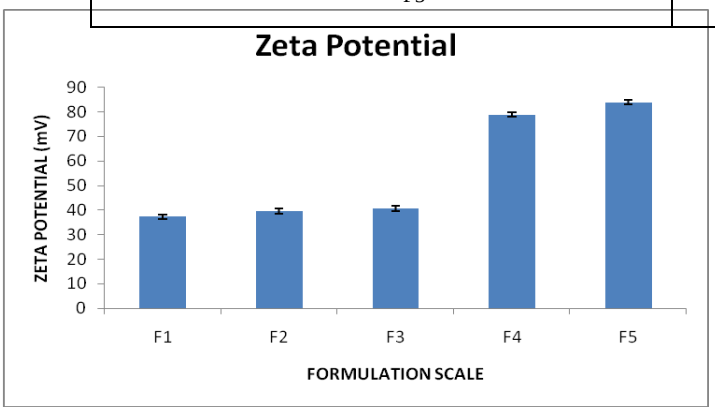

Figure: 3 Graph of Zeta Potential

All the nanoformulation has a positive average. The charge of positive due to, the positive charge of chitosan. The zeta potential of around 37.3 to 78.9 mV represents physically stable.

Entrapment Efficiency

Entrapment efficiency of montelukast sodium was determined by calculation the Amount of drug in nanogel (mg) used to prepare the formulation and the amount of initial amount of drug added (mg) in the aqueous phase. Figure 4 is shown below representing the percentage drug entrapment Comparisons of the optimization parameters for different formulation are tabulated in Table 4.

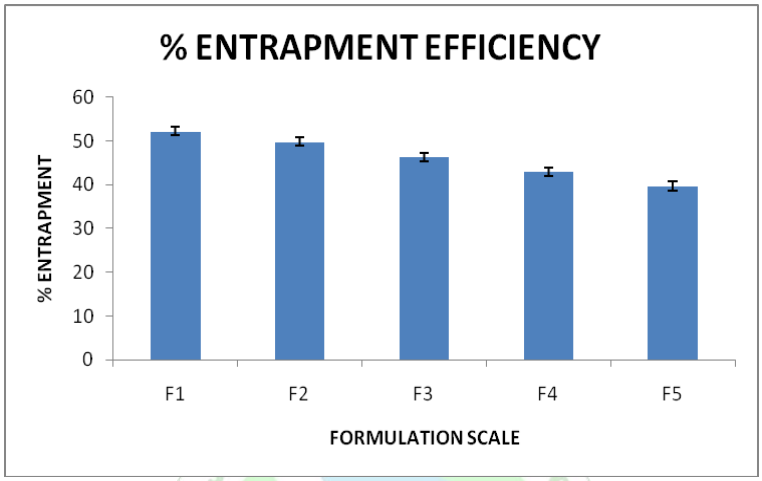

Figure: 4 Graph of % Entrapment Efficiency

Table 4: Formulation optimization with different parameters

Formulation code	Z average (nm)	PDI	Zeta Potential(mV)	Entrapment Efficiency (%)
F1	113.6±7.2	0.402±0.032	37.3±1.5	56.2±7.6
F2	206.9±9.6	0.503±0.058	39.6±1.2	54.5±6.9
F3	327.2±11.3	0.419±0.023	40.7±1.1	48.9±4.4
F4	649.3±15.2	0.426±0.049	78.9±0.8	44.7±3.5
F5	739.0±15.6	0.485±0.051	83.9±0.5	39.6±3.1

The entrapment efficiency of Nanoformulation was observed between 39% and 56% respectively with drug ratio. It was also observed that an increased drug concentration yield low encapsulation efficiency and larger particle size. The reason behind is that increased drug concentration result in bigger Nanogel.

In-vitro Drug Release

In-vitro ondansetron release from the nanogel was studied under a physiological condition (PBS, pH6.8) at 37◦C temperatures through cellulose membrane. Drug release study is an important tool which is very useful for quality control and also for the prediction of in- vivo kinetics.Here we have carried out the release study at 37 ◦C which is physiological body temperature.

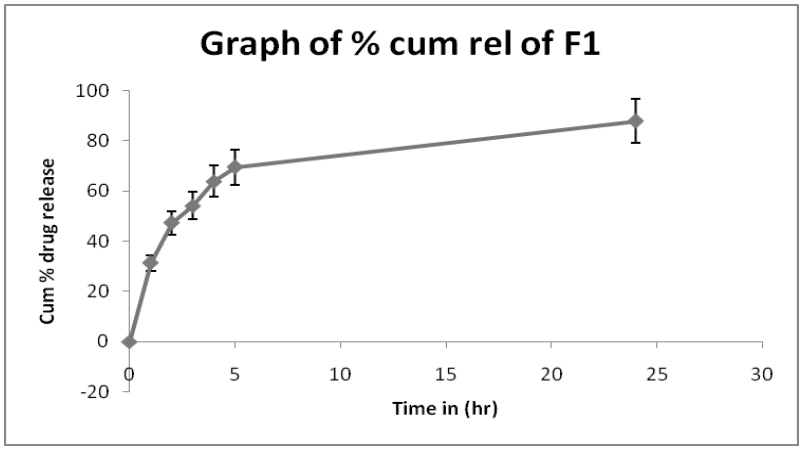

Figure 5: Cumulative % DrugReleaseofF1 Formulation

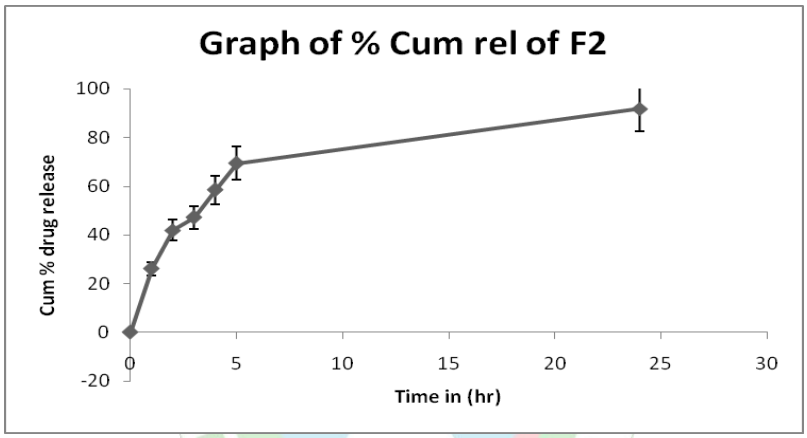

Figure 6: Cumulative % Drug Release of F2 Formulation

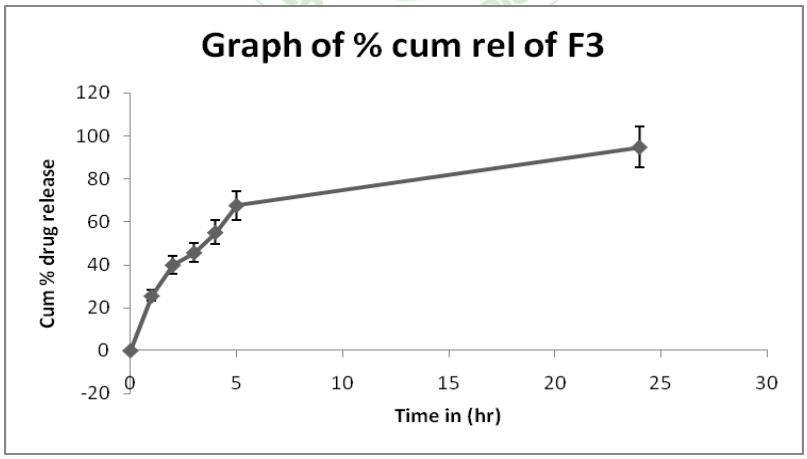

Figure 7: Cumulative%DrugReleaseofF3 Formulation

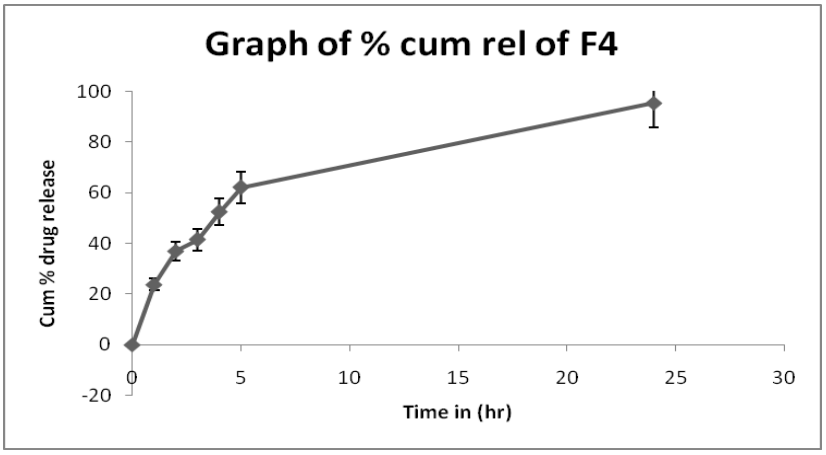

Figure 8: Cumulative % Drug Release of F4 Formulation

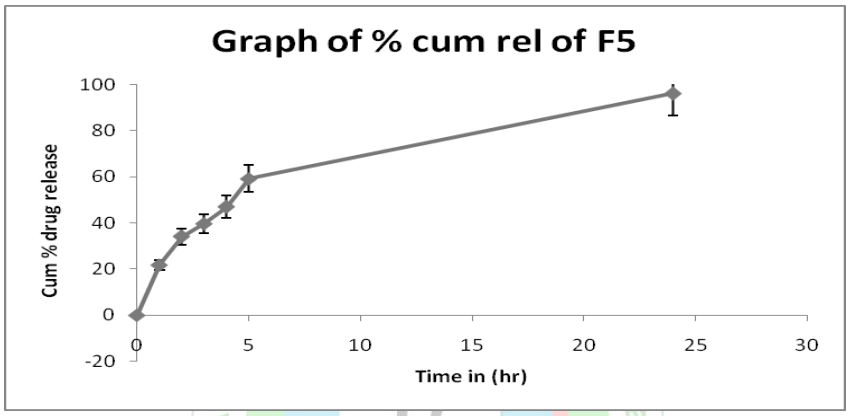

Figure 9: Cumulative % Drug Release of F2 Formulation

Clarity Test

Clarity test observed by visual inspection, all the formulation seen clear in appearance.

Table 5: Clarity Test of Nanogel Formulation

Formulation code	Appearance
F1	Clear solution
F2	Clear solution
F3	Clear solution
F4	Clear solution
F5	Clear solution

pH test of gel

pH of gel formulation observed by digital pH meter were range between 6.4.-6.84 which is considerable to avoid the skin irriation of skin after application.

Table 6: pH testof Nanogel Formulation

Formulation code	pH
F1	6.40
F2	6.68
F3	6.80
F4	6.84
F5	6.65

Viscosity

The measurement of viscosity of the prepared nanogel was done using the Brookfield viscometer F5 formulation showed better viscosity as compared to other formulations.

Table 7: Viscosity of Nanogel Formulation

Formulation code	Viscosity (Cps)
F1	14,600
F2	26,200
F3	32,200
F4	33,300
F5	35,300

Measurement of Gelation Temperature

The gelation temperature determined by using modified Miller and Donovan technique observed between range 20 – 28 ◦C.

Table 8: Measurement of Gelation Temperature of Nanogel Formulation

Formulation	Gelation Temp. (°C)	Gel melting Temp. (°C)
F1	28	80
F2	25	84
F3	23	87
F4	21	91
F5	20	94

SUMMARY AND CONCLUSION

Nanogel is the emerging traits to develop novel drug delivery system in this time because of their smart working property. The aim of this work was to take advantage of nanogel of Montelukast for the treatment of asthma and allergy by observing the behaviour of drug ratio. It is a novel and interesting strategy to work using chitosan as polymer for the prepation of nanogel. nanogel have the property of swelling which is of great usefulness for biological applications. It shows better drug loading and release as well.

In the pre-formulation study, there was not any physicochemical interaction between drug and polymer had been evaluated by FTIR. The melting point was found to be 134- 137 0C. It is freely soluble in Cyclohexane & butanol ratio and water. The standard curve of ondansetron had been prepared by Cycloheaxxane & butanol (7:3).

Montelukast nanogel were prepared by nanodispersion method. Formulations of different drug ratio were optimized with selected parameters like particle size, PDI, Zeta potential, entrapment efficiency, clarity test. pH test of gel, viscosity and gelation temperature. Influence of varying drug ratio was observed on particle size and it was found that 107.9±7.2. of formulation F1. The drug concentration increases there is an increase in particle size. Percent drug entrapment was evaluated and found to be decreasing with increasing drug ratio. The highest entrapment was found to be 52.2±7.6 with formulation F1. On the basis of particle size and entrapped efficiency of F1 formulation was decide as optimized formulation.

Drug release studies were performed by dialysis bag diffusion technique at a temperature (37°C). The study was continued for 24 hours till. The maximum amount of drug montelukast release 87% within 24 hr. The study was monitored at 37°C. Preparation, characterization and drug release study of montelukast loaded nanogel.

The results of the study are montelukast nanogel used for developing the more advantageous drug delivery system.Montelukast nanogel is more favorable for biomedical applications which definitely make an impact in the medical field. It is beneficial to reduce the frequent dosing thus enhance bio patient compliance and half-life. This allows us to aim for further improvement in the montelukast nanogel formulation for better treatment of asthma and allergy by topical delivery. This approach of montelukast loaded nanogel with chitosan as the polymer is quite successfully developed.

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