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FORMULATION AND EVALUATION OF DEFLAZACORT NANOCAPSULE FOR CROHN'S DISEASE

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ABSTRACT

Nanocapsules can be compared to vesicular systems in which the drug is trapped in a cavity that encloses an internal fluid surrounded by a polymeric membrane. Nanocapsules show promise as active vectors because of their ability to release drugs; their small cell size allows for higher intracellular acquisition than other particle systems.

The nanocapsule can be directed to specific cells and areas within the body after intravenous and subcutaneous injections. The formation of a nanocapsule is a mixture between a polymeric nanocapsule and a liposome due to its oily substance surrounded by a strong pressure-acting membrane. The advantage of the encapsulation method is to protect these objects to be protected in the wrong place, to be controlled and precisely identified.

Deflazacort is a glucocorticoid with a high glucocorticoid receptor affinity but low systemic function due to excessive initial metabolism in the liver. Deflazacort has a short half-life from 1.1-1.9 hours. So it is ready for further release. Lipidic nanocapsule was developed that will provide greater stability and reduce drug toxicity.

Keywords: Nanocapsules, Deflazacort, Liposomes, Glucocorticoids

INTRODUCTION

Nanocapsules can be likened to vesicular systems in which a drug is confined in a cavity consisting of an inner liquid core surrounded by a polymeric membrane. It can be defined as Nano-vesicular systems that exhibit a typical core-shell structure in which the drug is confined to a reservoir or within a cavity surrounded by a polymer membrane or coating. Nanocapsules, existing in miniscule size, range from 10 nm to 1000 nm. Nanocapsule show promise as active vectors due to their capacity to release drugs; their sub cellular size allows relatively higher intracellular uptake than other particulate systems.

The nanocapsule can be targeted to specific cells and locations within the body after intravenous and subcutaneous routes of injections. Nanocapsules comprise of an oily or an aqueous core, which is surrounded by a thin polymer membrane. The nanocapsule core may be aqueous or composed of lipophilic solvent usually oil. The structure of nanocapsule is a hybrid between polymeric nanocapsule and liposome because their oily core which is surrounded by a tension-active rigid membrane. The benefit of encapsulation method are of protection of these substances to protect in the adverse environment, for controlled release and for precision targeting.

COMPONENT OF NANOCAPSULE:

- ❖ Lipids
- ❖ Oils
- ❖ Surfactant
- ❖ Water

METHOD OF PREPARATION OF NANOCAPSULE:

- ❖ Emulsification-diffusion
- ❖ Nano-precipitation
- ❖ Emulsification-conservation
- ❖ Layer by layer
- ❖ Phase inversion
- ❖ Solvent evaporation
- ❖ Double emulsification

CONTROL RELEASE DRUG DELIVERY

Controlled dosage forms cover a wide range of long-acting action that provides continuous release of its ingredient at a predetermined time.

The goal of any drug delivery system is to provide the right amount of medication to the body so that you can get the fastest and maintain the required drug dosage which the drug delivery system must deliver the drug at a price indicated by the body's needs. within the prescribed period of treatment. The two components of the placement of drug delivery and the temporary delivery of the drug. Location

placement is related to the identification of a drug in a particular organ or tissue, while temporary delivery refers to controlling the level of drug delivery to a specific organ. It is the one that quickly reaches the desired medical focus and remains the same throughout the course of treatment..

ADVANTAGE OF CONTROL RELEASE:

- ❖ Optimal use of drug and improve the patient compliance.
- ❖ Controlled rate and site of release.
- ❖ Reduced dose frequency.
- ❖ Improved patient compliance.
- ❖ The maintenance of drug level within a desired range.
- ❖ Better drug utilization.
- ❖ Decrease toxicity.
- ❖ More consistent and prolonged therapeutic effect.

DISADVANTAGE OF CONTROL RELEASE:

- ❖ Stability problem.
- ❖ Undesirable by product of degradation.
- ❖ The chance of patient discomfort from the delivery device for instance if any surgery required to implant or remove the system.
- ❖ Higher cost of controlled release system compared with traditional pharmaceutical formulation.
- ❖ Toxicity due to dose dumping.
- ❖ More rapid development of tolerance.
- ❖ Increased Cost.

INFLAMMATORY BOWEL DISEASE (IBD)

IBD is a group of inflammatory conditions of the colon and small intestine. IBD is class of auto immune disease, in which the body's own immune system attacks the elements of the digestive system.

Two major types of inflammatory bowel diseases are ulcerative colitis and crohn's diseases.

- ❖ Ulcerative colitis: it involves only the colon starting from the anal canal. It can remain restricted to the rectum or extended proximally in a contiguous manner to variable extent upto caecum. The lession are mucosal and may be diffuse or confluent. The first definitive description of this condition was made in **1909** and in certain aspects it resembles Crohn's diseases
- ❖ Crohn's disease: in crohn's diseases lesions are patchy and transmural; may involve any part of the g.i.t from mouth to the anus .majority of patient have ileocaecal diseases upto ascending colon , but in some it may be restricted to the small intestine . Because the lesions are transmuara, complication like perforation, abscess, fistula, strictures, etc.

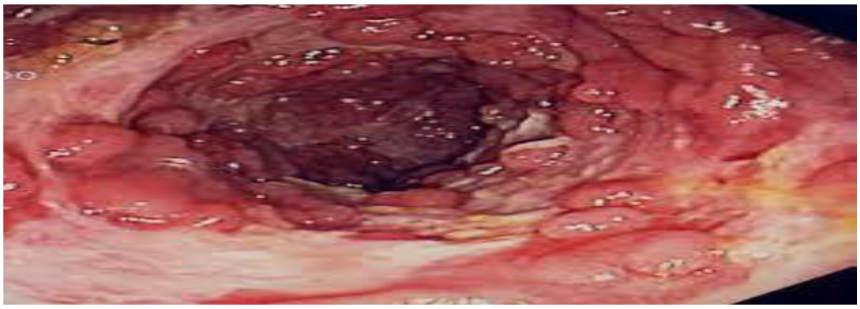


Figure 1: Inflammation in colon

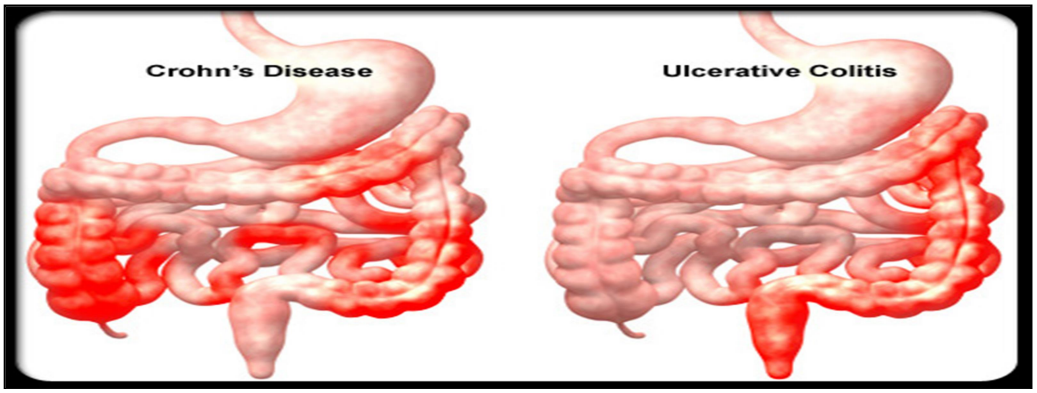


Figure 2: Different location of Crohn's disease and ulcerative colitis

SYMPTOMS OF INFLAMMATORY BOWEL DISEASES:

Diarrhea

Abdominal pain and cramping

Mouth sores

Fever and fatigue

Blood in your stool

Reduced appetite and weight loss

TREATMENT AND DRUG USE IN IBD:

Anti-inflammatory drug

- 5-amino salicylic acid (5-ASA)compound
- Corticosteroid
- Immunosuppressant

Sulfasalazine: These drug may be help in crohn's disease affect the colon, but they aren't helpful in treating in the small intestine. They include sulfasalazine which contain sulfa, and mesalmine. The beneficial effect of sulfasalazine is clearly not due to any antibacterial action. The sulfapyridine emoiety only serve to carry 5-ASA to the colon without being absorbed proximally. Most of the adverse effectlike nausea, fever, joint pain, headache, malaise and anaemia etc. Higher dose of mesalmine may induce remission in mild cases of Crohn's colitis as well, but efficacy is uncertain. It is not useful in maintaining remission in Crohn's disease.

Corticosteroid: Corticosteroid such as prednisolone can help in reduces inflammation anywhere in your body, but they have numerous side effects, which include a puffy face, excessive facial hair, hyperactivity .more serious side effects include diabetes, cataracts, and glaucoma. Deflazacort work by reducing inflammation in the colon. Doctor's generally use them only if you don't respond to other treatment.

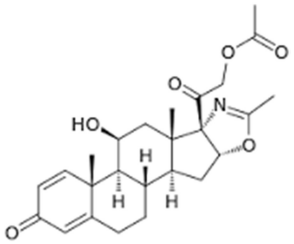
Immunosuppressant: They are used for long term management of IBD. For eg. Azathioprine, this purine metabolite is the most effective use immunosuppressant in IBD. Some patient experience bone marrow toxicity of azathioprine.

Drug: Deflazacort

Deflazacort is a synthetic steroid that has an anti-inflammatory effect. It is used to decrease inflammation in various different diseases and conditions. Also use in inflammatory bowel disorder such as crohn's diseases and in ulcerative colitis.

Deflazacort is glucocorticoids that have high affinity for the glucocorticoid receptors but low systemic activity due to extensive first pass metabolism in liver.

Table 1: Drug profile:

Sr. No.	Parameter	Deflazacort
1	Molecular Formula	$C23H29NO_4$
2	Structure	
3.	Molecular Weight	441
4.	Appearance	White to off white, crystalline structure
5.	IUPAC Name	11β,16β)-21-(acetyloxy)-11-hydroxy-2′-methyl-5′H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione
6.	Category	Corticosteroid
7.	Mechanism	Deflazacort is an inactive prodrug which is metabolized rapidly to the active drug 21-desacetyldeflazacort
8	Route of administration	Oral
9.	Bioavailability	60%
10.	Protein binding	~40%
11.	Half life	1.1 – 1.9 hours
12.	Melting point	255-258
13	Log p	1.06 (±) 0.66
14.	Pka	9.87
15.	Water solubility	Insoluble
16.	Dose	6mg
17.	Excretion	70%

MATERIALS USED IN PRESENT WORK:

Table 2: Materials used in Present Work		
Category	**Materials & reagents**	**Supplier**
Drug	**Deflazacort**	**Qp pharmachem Ltd**
Lipid	**Cholesterol**	**SD fine,Ltd**
	Lecithin 100	**Sigma Aldrich Chemical. Pvt ,Ltd**
	Lipoid S 75	**Lipoid , Germany**
Organic solvent Oils	**Ethanol**	**SD fine .Ltd**
	Methanol	**SD fine .Ltd**
	Olive oil	**SD fine .Ltd**
Surfactant	**Ethyl oleate**	**SD fine .Ltd**
	Oleic acid	**SRL**
	Castor oil	**SRL**
	PEG 600	**SD fine .Ltd**
	Cremophore RH 40	**Sigma Aldrich Chemical. Pvt ,Ltd**
	Tween 80	**SRL**
NON SOLVENT	**Water**	**Water supply specialist Pvt .Ltd, vadodara, India**
	Nacl	**Fisher**

EQUIPMENT'S USED IN PRESENT WORK:

Table 3: Equipments used in Present Work	
Equipments	**Manufacturer**
Digital weight balance	**Scaletec Mechatronic Pvt.Ltd.**
Magnetic stirrer	**Remi Service Pvt. Ltd.**
Mechanical stirrer	**Remi Service Pvt. Ltd**
Lyophillizer	**Allied Frost, New Delhi**
Malvern zeta seizer	**Nano ZS-90 Malvern Instrument UK**
U.V Visible spectroscopy	**Shimadzu 1800, Japan**
Scanning electron microscope	**FEI SEM**
Fourier Transform infrared spectrophotometer	**Bruker Alpha,Germany**
Dissolution test apparatus	**LAMBINDIA DS 8000**
Stability chamber	**Remi Instrument Ltd,Mumbai**

SUMMARY OF EXPERIMENTAL WORK:

1) Preformulation study
   a) Solubility study
   b) Melting point determination
   c) FTIR spectra of Budesonide
   d) Compatibility study by FTIR
2) Calibration curve development
3) Preparation of Lipid nanocapsule
   a) Screening of Lipid
   b) Screening of Oil
   c) Screening of Surfactant
   d) Factorial design
   e) Check point batch preparation
4) Characterization & evaluation of optimized Lipid nanocapsule
   a) Particle size & Polydispersity index
   b) Zeta potential
   c) Encapsulation efficiency
   d) Drug content
   e) Scanning electron microscopy
5) In vitro study
6) Stability study

PRE-FORMULATION STUDY:

IDENTIFICATION OF DRUG:

Organoleptic Property: As per Indian pharmacopeia 2014 drug was white colour having crystalline structure

Solubility Study: 10 mg drug was taken in the test tube and solvent was added gradually in volume of 10 ml with continuous shaking until it dissolves completely. Solubility of drug was checked in water, ethanol, methanol and acetone. Solubility was calculated as per descriptive term given in Indian Pharmacopeia 2010.

Table 4: Solubility study

Sr. No.	Descriptive terms	Parts of solvent required for part of solute (gm/ml)
1.	Very soluble	Less than 1
2.	Freely soluble	From 1 to 10
3.	Soluble	From 10 to 30
4.	Sparingly soluble	From 30 to 100
5.	Slightly soluble	From 100 to 1000
6.	Very slightly soluble	From 1000 to 10,000
7.	Practically insoluble	10,000 or more

MELTING POINT DETERMINATION:

Melting point of Deflazacort was determined by capillary method using melting point. Powdered drug was poured in one side open end of thin capillary about 5cm length with uniform diameter by tapping gently. Capillary was the placed into the orifice of the melting point apparatus (VERGO Model VMP-D) the temperature at which solid start melting and completely converted into liquid state that temperature is recorded as a digital display and recorded as a melting point of a drug.

IDENTIFICATION BY FTIR:

The FTIR of drug and lipid ,drug +oil and drug +surfactant were performed using Fourier transform infrared spectrophotometer (BRUKER ALPHA –T) and the physical mixture of drug and all excipient is mixed with KBR pellet scanning is done from 400 to 4000cm^{-1}.

DIFFERENTIAL SCANNING COLORI-METRY:

Differential Scanning Calorimetry was used to evaluate the thermal behaviour of pure drug and Nanocapsule formulation. Samples were taken and sealed in standard aluminium pans and then scanned range from 25 to 350 C at a heating rate of 10.00°C/min, in the presence of nitrogen atmosphere

PREPARATION OF PHOSPHATE BUFFER PH 6.8:

The ingredient mentioned in Table were weighed accurately and dissolved in 1000 ml of distilled water and pH was adjusted to 6.8.

Table 5: Formula for phosphate buffer pH 6.8	
Ingredient	**Quantity**
Di sodium hydrogen phosphate	**28.8 g**
Potassium hydrogen phosphate	**11.45 g**
Distilled water	**1000 ml**

ANALYTICAL METHOD FOR ESTIMATION OF DEFLAZACORT:

Preparation of 0.1N HCl: Diluting 8.5 ml of HCl to 1000 ml with distilled water to preparing 0.1N HCl

Prepartion of 6.8 phosphate buffer: dissolve 6.80 g of monobasic potassium phosphate and 0.46g of sodium hydroxide into 1 litre to a suitable container .Adjust with 1 N sodium hydroxide and mix well.

Determination of λ max of Deflazacort in 0.1 N HCl : 10 mg Deflazacort was dissolved in 10ml Methanol and the volume is make up with 0.1 N HCL in 100 ml of volumetric flask to form (100µg/ml).sonicate it for 5min .from that stock solution withdrawn 1 ml and dilute it with 0.1 N HCl form 20 ppm solution . Then, it was observed by UV-Visible spectrophotometer (Shimadzu 1700, Japan) in spectrum mode to get spectra of Deflazacort in which wavelength maxima was determined. The spectrum was run between 200-400 nm.

Determination of λ max of Deflazacort in 6.8 phosphate buffer [(34)]: same procedure willdofor 6.8 pH phosphate buffer and in UV visible spectrophotometer in spectrum mode the scanning is done. The spectrum is run between 200-400 nm.

Prepartion of Calibration curve of deflazacort in 0.1N HCl:10mg of drug was dissolved in 10 ml of methanol in 100ml volumetric flask and make up the volume with o.1 N HCL (100 µg/ml) From above stock solution solutions aliquots of 0.8, 1.0, 1.2, 1.4, 1.6, 1.8, 2.0ml was withdrawn which was diluted up to 10ml with 0.1 N HCl. Resulted solution will form 8, 10, 12, 14, 16, 18, 20 µg/ml respectively. Above solution was measured in UV-Visible Spectrophotometer at 246 nm.

Prepartion of calibration in 6.8 pH phosphate buffer: 10mg of drug dissolved in 10ml of methanol then make up the volume with PB pH 6.8 form in 100 ml of volumetric flask (100 µg/ml) From above stock solution aliquots 4, 6, 8, 10, and 12 ml was withdrawn which was diluted up to 10ml with PB pH 6.8 Resulted solution will form 6, 8, 10, 12, and 14 µg/ml respectively. Above solution was measured in UV-Visible Spectrophotometer at 246 nm.

Selection of excipients:

Screening of oils: Formulation is prepared by checking the solubility of drug in various oil. Take 10 mg of drug and placed in 10 ml of various oil and put them in the orbital shaker for 24 hrs. After that the absorbance is taken by UV visible spectrophotometer highly soluble oil is optimized.

Screening of lipids: formulation is prepared by using different lipids, oil and surfactant at different concentration. Then the selection of lipid is done by trial batches and evaluates its Particle size, PDI and entrapment efficiency, then optimize the formulation by particle size and entrapment efficiency.

Screening of surfactant: formulation is prepared by taking different concentration of surfactant in different batches. Then optimization is done by particle size and entrapment efficiency

Drug excipient compatibility study: The FTIR of drug and lipid ,drug +oil and drug +surfactant were performed using Fourier transform infrared spectrophotometer (BRUKER ALPHA –T) and the physical mixture of drug and all excipient is mixed with KBR pellet scanning is done from 400 to 4000cm^{-1}

Differntial Scanning Calorimetry compatibility study: The DSC of Nanocapsule formulation were performed using the model STAR Default DBV1300. METTLER. The scanning is done from 25 °C to 350°C.

Evaluation of lipid Nanocapsules:

Particle size, polydispersity index

The average particle size and polydispersity index of lipid nanocapsule was determined by photon correlation spectroscopy using zetasizer Nano ZS90 (Malvern instrument) each sample was diluted with distilled water.

Zeta potential:

Zeta potential was determined using zetasizer. Clear disposable zeta cell cuvette was used for determining zeta potential. The cuvette was filled using micro pipette .20 zeta runs made for each sample and temperature was maintained at 25°C.

Entrapment efficiency: Entrapment efficiency percent (EE %) was determined by measuring the concentration of Unentrapped free drug in aqueous medium. The aqueous medium was separated by centrifugation. By measuring an amount 1.5ml of the LNC dispersion was placed in the Eppendorf Amicon Ultra centrifugal filters with cutoff 10 KDa and centrifuged at 15000 rpm for 10 min the concentration of deflazacort in the aqueous phase was determined using UV-visible spectrophotometer at λmax 246 nm.

% EE was calculated using following equation:

$$\%EE = \frac{\text{Drug content in nanocapsule}}{\text{Total content of used drug}} \times 100$$

Drug content: The formulation obtaining 100 mg equivalent quantity of drug was taken in 100ml volumetric flask, dissolved in Phosphate buffer pH 6.8 and the volume is make up with 100ml of phosphate buffer pH 6.8 in 100ml of volumetric flask. The absorbance was measured with suitable dilution at 246 in triplicate. And the concentration were calculated from standard calibration curve prepared in phosphate buffer pH 6.8

Scanning electron microscopy: The surface morphology of the optimized formulation were obtained from SEM images. The surface morphology and appearance of the particle size were observed at X2700 magnification and an accelerating voltage of 15kV.

In vitro release study: In vitro release of deflazacort from lipid nanocapsule formulations was determined by dialysis nag method by USP type II (Paddle type) dissolution apparatus to study the effect of pH on drug release. The release studies were performed in 0.1 N HCl and in 6.8 ph phosphate buffer. Dialysis bag having pore size 2.4nm and molecular weight 14000 (dialysis membrane 150, Hl Media, Mumbai India) was used. The bag was soaked in buffer solutions 24hours before use. To determine the release rate of Deflazacort from lipidic nanocapsules 2ml of lipid nanocapsules was placed in dialysis bag and sealed at both ends. In 900ml of 0.1 N HCl for 2 hrs. And phosphate buffer 6.8 for 8 hrs with 100 rpm at ±Samples were withdrawn with predetermined time interval and the sink condition is maintained by replaced with fresh PBS maintained at the same temperature. The content of Deflazacort in the samples was determined at λmax 246 nm.

Release kinetics of Lipid Nanocapsules:

The study release kinetics of deflazacort from lipid nanocapsule , the release data were fitted to following equation :

Zero order kinetics:

$f1=K0t$

where f1= fraction of dose release at time t

K0= zero order release rate constant

First order kinetics:

$lnQt= ln+ Kt$

Where, Qt= amount of drug remaining to be released at time t,

Q0 = amount of drug remaining to be released at Zero hour,

Kt= first order release rate constant

Higuchi model:

$Qt=KHt^{1/2}$

Where KH= Higuchi release rate constant

Hixon –crowell model:

$W0^{1/3} - Wt^{1/3} = Kst$

Where, W0= initial amount of drug present in matrix,

W1=amount of drug release at time t

Ks=Hixon Crowell release rate constant

Korsmeyer peppas model:

$Mt/M\infty = K\ t^{n}$

Where=amount of drug release at time t

M∞=amount of drug release at infinite time

K=Korsmeyer peppas released rate constant

n =release exponents

Table 6: Type of drug transport mechanism

The type of drug transport mechanism		
Diffusional Exponent ,n	**Type of transport (release)**	**Time dependent**
n =0.5	**Fickian diffusion**	**$t^{1/2}$**
n =>0.5-<0.1	**Anomalous transport**	**t^{n-1}**
n =>0.1	**Case II transport**	**time dependent**
n >1.0	**Super case II transport**	**t^{n-1}**

Ex -vivo permeation Study: Ex vivo study was conducted using isolated chick intestine. 10cm length of intestine was cut and washed by syringe and empty the residual content of intestine. One end of intestine tight with thread. From other open end filled with drug and 0.1 N HCl .Similarly the other intestine filled with optimized formulation with 0.1 N HCl. Both were placed in 50 ml beaker separately containing 50 ml Stimulated gastric fluid place in magnetic stirrer and 100 rpm. The amount of dug diffuse was find out by withdraw 2ml sample by 2 hour interval.

Stability Study: the stability study of optimized batch were performed as per ICH guidelines. The stability study of lipid nanocapsule were carried at 40° C /75% RH, 25° C/60% and 4°C

Phytochemical screening of collected gums

Molish's test for presence/ absence of Carbohydrates

Iodine test for presence/ absence of Starch

Benedict's test for presence/ absence of Reducing

Seliwanoff's test for presence/ absence of Ketose

Diphenylamine reagent for presence/ absence of Hexose

Tollen's test for presence/ absence of Aldehyde

Physicochemical characterization of gums

Solubility test

The separated gum was evaluated for solubility in water, acetone, chloroform and ethanol in accordance with the British pharmacopoeia specifications.

Swelling index

1.0g of powdered sample was placed in each of 15ml plastic centrifuge tubes and the volume occupied was noted.10ml of distilled water was added from a 10ml measuring cylinder and stoppered. The contents were mixed on a vortex mixer for 2 min. The mixture was allowed to stand for 10min and immediately centrifuged at 1000rpm for 10 min on a bench centrifuge. The supernatant was carefully decanted and the volume of sediment measured. The swelling index was computed using the equation:

$S = V_2 / V_1$.

Where; S = Swelling index, V_1 = Volume occupied by the gum prior to hydration, V_2 = Volume occupied by the gum after to hydration

Loss on drying

1.0g of the powdered sample was transferred into each of several Petri dishes and then dried in an oven at 105°C until a constant weight was obtained. The moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a percentage.

Total ash and acid insoluble ash determination

Ash content was estimated by the measurement of the residue left after combustion in a furnace at 450°C.The ash obtained from the determination of the ash was boiled with 25 ml of 2M hydrochloric acid solution for 5 minutes and the insoluble matter was filtered and washed with hot water and ignited and the subsequent weight was determined. The percent acid insoluble ash was calculated.

pH determination

This was done by shaking a 1%w/v dispersion of the sample in water for 5 min and the pH determined using a pH meter.

Angle of repose

The static angle of repose, a, was measured according to the fixed funnel and free standing cone method. A funnel was clamped with its tip 2cm above a graph paper placed on a flat horizontal surface. The powders were carefully poured through the funnel until the apex of the cone thus formed just reached the tip of the funnel. The mean diameters of the base of the powder cones were determined and the tangent of the angle of repose calculated using the equation:

$$\theta = \tan^{-1}(h/r)$$

where, θ = Angle of repose; h = height of the heap of pile and r = radius of base of pile.

Bulk and tap densities

2.0g quantity each of the powder sample was placed in a 10ml measuring cylinder and the volume, V_0 , occupied by each of the samples without tapping was noted. After

100 taps on the table, the occupied volume V_{100} was read. The bulk and tap densities were calculated as the ratio of weight to volume (V_0 and V_{100} respectively).

Hausners index

This was calculated as the ratio of tapped density to bulk density of the samples.

Compressibility index (C%)

This was calculated using the equation:

Compressibility = (Tapped density − bulk density)/Tapped density × 100.

Fourier Transform Infra Red (FT-IR)

The FT-IR spectrum of the sample was recorded in an IR spectrometer using potassium bromide (KBr) discs prepared from powdered samples mixed with dry KBr in the ratio 1 : 200. Triplicate measurements were made, and the spectrum with the clearest identifiable peaks was chosen.

Summary :

Deflazacort is a glucocorticoid use in the treatment of inflammatory bowel diseases. In which two condition are there crohn's diseases and ulcerative colitis. The aim of the present study was to development and evaluation of Deflazacort Nanocapsules of for the treatment of inflammatory bowel diseases. The solubility of drug was found in different solvent i.e water, methanol, 6.8 ph phosphate buffer and 0.1 N HCl . and the screening of lipid and surfactant is done on the basis of particle size and entrapment efficency. The oil is selected on the basis of solubility profile. UV spectroscopy method is used for the analysis of drug and calibration curve is plotted and the linearity is found from the curve. Melting point of drug was determined by using Melting point apparatus method.

Olive oil gives the highear solubility in which 10 mg of drug is taken ans added into 10 ml of oil. Then kept in the orbital shaker for 24 hours and then centrifugation is done and then finally measuring its concentration using UV spectroscopy it gives highest solubility of drug so olive oil was selected.Lipoid S 75(70% phosphatidlycholine) is selected on the basis of Particle size and polydispersity index. And Tween 80 is selected also selected on the basis of particle size and its PDI it shows nanometer size range, therefore it was selected. All these selected are taken and development of nanocapsule is done by using Phase –inversion method.

IR spectroscopy of drug was recorded and its functional group was determined and interpretation is done by the structure of drug . IR spectra of individual excipient is performed and physical was performed containning drug and compatibility study was done. DSC study was also performed for

pure drug and Nanocapsule formulation and its compatibility study was done.

Total all seventeen batches werer prepared using Box-Behnken design with three independent variable Oil,surfactant,Lipid were taken and two dependent response was evaluated by particle size , % entrapment efficencency also evaluation of Zeta potential , drug content , in vitro drug release study was carried out for optimized batch .

All the Lipidic Nanocapsule shows that the particle size in the range of 41-89.00 and the zeta potential shows that the formulatiomn was stable.and entrapment efficency is in the range of 44.1-80.Scanning electron Microscopy shows that particles are in crystalline shape and smooth surface was found. In vitro release gives the sustain release profile and kinetic study for the optimized formulation was done.

Ex-vivo study was done for the comparision of pure drug and Nanocapsule formualtionof the optimized batch. And the optimized formulation gives the grater release in comparision of pure drug . and finally stability study was performed for the optimized batches at 4 C, 25 C, 40 C for 1 month.

CONCLUSION:

The Lipidic Nanocapsule made from Lipid layer and the drug i.e: Deflazacort was incorporated in the inner core of the lipid layer.Screening of oil, surfactant and lipid were done for the selection of Excipients. The phase inversion method was used for the preparation of Lipidic Nanocapsuleand it was converted into Dry powder by the help of Lyophillizer. Formulation of Lipidic Nanocapsule eas done by using Box-Behnken Layout .and the optimized batches F12 gives the particle size 45.42 and gives % 81.25Entrapment efficency . The optimized formulation having highest entrapment efficency.

Drug and excipients Compatibility study shows the interaction between drug and Exipients.so its performed by FTIR and by using DSC. And the DSC of the formulation was also performed. The formulation is followed the Kors-meyer peppas model and the formualtion gives the sustain release. Ex-vivo study was done for the comparision study between drug and optimized nanocapsule formualation.it will increases the permeation and it shows the grater release as compared to pure drug . Thus the formuation of Deflazacort Lipidic Nanocapsule is better candidate for oral drug delivery system.

REFERENCES:

[1] Catarina Pinto Reis, Ronald J. Neufeld, Antonio J. Ribeiro, C

Francisco Veiga, "Methods for Nanoencapsulation for the prepartion of drug loaded polymeric Nanoparticles" Nanomedjournal. 2006, (2), 8– 21.

[2] Dineshkumar B, Krishnakumar, Anish John, David Paul, Joseph Cherian, L. Panayappan. "Nanocapsules a Novel Nano-Drug Delivery System". Int .journal of research in drug delivery.2013,3,1-3.

[3] Satyanarayan Pattnaik, Kalpana Swain, Jupally Venkateshwar Rao1, Sanjeev Kumar Subudhi. "Pharmaceutical Nano-encapsulation strategies: a mechanistic review". Int journal of pharmacy and biological science. 2012, 280-284.

[4] Nilesh jain,Ruchi J,Naveen T,Brahmprakash G, Deepak kumar J, Jeetendra banveer, Surendra jain."Nanotechnology: a safe and effective drug delivery system". Asian Journal of Pharmaceutical and Clinical Research.2010,3 ,0974-2441.

[5] Suresh P. Vyas, Roop K. Khar. Controlled drug delivery, 7th Edition Vallabh Prakashan, New Delhi. 2012, 6-11.

[6] Jain N.K, Controlled and Novel Drug Delivery; 1st edition, CBS publishers and Distributors, Delhi, 1997, 292-301.

[7] KD Tripathi .Essential of medical Pharmacology; 7th edition; Jaypee brothers Medical Publisher New delhi 2013,683-685.

[8] Inflammatory bowel disease", September 2014, http://en.wikipedia.org/wiki/Inflammatory_bowel_disease

[9] "Inflammatory bowel disease", October 2014, https://gi.jhsps.org/GDL_Disease.aspx

[10] "Crohn's disease", September 2014, http://en.wikipedia.org/wiki/Crohn's_disease

[11] "Ulcerative colitis", September 2014, http://en.wikipedia.org/wiki/Ulcerative_colitis

[12] Drug.com. Deflazacort Deflazacort September 2015, www.drugupdate.com

[13] Deflazacort: September, Drug information 2015.

[14] www.netdoctor.co.uk/seniorshealth/medicines/calcort tablets.

[15] Deflazacort: Sep 23, 2015. www.akesissindia.com/delzy.

[16] Paola Sanchez-Moreno, Houria Boulaiz, Juan Luis Ortega-Vinuesa,

Jose Manuel Peula-Garcia, and Antonia Aranega. "Docetaxel loaded nanocapsules as a Novel Drug Delivery system as a therapeutic strategy against Breast Cancer Cells."Int. J. Molecular science. 2012, 13, 4906-4919.

[17] Benjamin Saliou, Olivier Thomas, Nolwenn Lautram, Anne Clavreul, Jose Hureaux, Thierry Urban, Jean Pierre B, Frederic Lagarce. "Development and in vitro evaluation of a novel lipid nanocapsule formulation of Etoposide" European Journal of Pharmaceutical Sciences. 2013, 172-180.

[18] AC Groo, M Bossiere, L Trichard, P Legras, JP Benoit, & F Lagarce. "In vivo evaluation of paclitaxelloaded lipid nanocapsules after intravenous and oral administration on resistant tumor". J. of nanomedicine."2015, 10,589-601.

[19] Catarina P, PhD, Ronald J. Neufeld, Antonio J. Ribeiro, Francisco Veiga, "Nanoencapsulation methods for preparation of drug-loaded polymeric nanoparticles". Nanomed journal.com. (2006), 2, 8– 21.

[20] Vijaya Kumar D, Premalatha, Ramesh K, M, Raj Kumar, "Formulation and evaluation of Deflazacort controlled release tablets Pelagia research library.com. 2011, 2 (4)78-86

[21] Davidquintar –guerrero, Ericallemann, eric Doelker, and Hatemfessi. "Preparation and characterization of nanocapsule from preformed polymer by a new process base on emulsion diffusion technique." J. of pharmaceutical research. 1998, 15-20

[22] Yadav Kumar Suresh, Niranjan SK, Jain SK, Maurya Sateesh, Kumar Vinay, " Design and development and evaluation of Mouth dissolving tablets of Deflazacort using Super disintegrants." World journal of pharma and pharmaceutical sciences. 2013,2, 5552-5568

[23] Preeti Gawde, Shikha A, Prabhat Jain, "Development of Muco-adhesive Microsphere for Colon Delivery". Int. journal of Pharmaceutical & Biological Archives. 2012, 3,440-442.

[24] Jyoti Wadhwa, Abhay Asthana, Sumeet Gupta, Gyati SA, and Ranjit Singh, "Development and

Optimization of Polymeric Self-Emulsifying Nanocapsules for Localized Drug Delivery design of Experiment Approach", The Scientific World Journal. 2014, 1-12

[25] Paola S.M, Juan Luis O.V, Antonio Martin-R, Houria Boulaiz, Juan Antonio Marchal-Corrales and Jose Manuel Peula-Garcia. "Characte-rization of different functionalized lipidic Nano-capsules as a potential Drug Carriers."Int. J. of Molecular Sciences.2012, 13, 2405-2424

[26] Scheila R Schaffazick, Adriana R. Pohlmann, Graziela Mezzalira I, Silvia S. Guterres, "Development of nanocapsule suspensions and nanocapsule spray dried powders containing melatonin." J. of the Brazilian Chemical Society. 2006, 17, 1678-4790.

[27] Mosqueira VC, Legrand P, Pinto Alphandary Mosqueira VC , Legrand P, Pinto Alphandar H, Puisieux F, Barratt G. Poly (D, Llactide), "Prepartion of Nanocapsules by solvent displacement method and its influence of the composition on Physico-chemical and Structural properties", J.Pharm Sci., 2000, (5),614-26.

[28] Alexander Mullen, Howard Stevens, Sarah Eccleston. Delayed prolong drug delivery. USPTO, US20130022677 A1, 2013

[29] Petit Josep Lluis Viladot, Gonzalez Raquel Delgado, Botello Alfonso Fernandez. World wide. Espacenet.com Nanocapsule containing Micro-emulsion. EP 2618926 A2, 2013

[30] Beatrice Heurtault. Lipid-nanocapsule preparation and process and use as medicine. World wide. Espacenet.comUS8057823 B2, 2011

[31] Hoarau, Didier, Montreal, quebec. World wide.Espacenet.com Stealth lipid nanocapsule , Method for the preparation thereof and the use thereof as a carrier for active principles, WO 2003, 103822, 2005

[32] David Quintanar, Hatem Fessi, Eric, USPTO, Method to prepare vesicular nanocapsule, WO99/ 04766, 2005.

[33] Pavia DI. In spectroscopy ;Indian edition; Cengage Learning Page no 979-981

[34] Satish A Patel, "Development and validation of spectrophotometric methods for determination of

deflazacort in Pharmaceutical dosage form" Int. Journal of Pharmacy and Pharmaceutical Sciences. 2011, 3.

[35] Patel Satish A and Patel Natvarlal J. "High performance thin layer chromatographic method for estimation of deflazacort in tablet". J. of Applied Pharmaceutical Science.2011, 7, 94-98.

[36] Ibrahima Youm, Xiao Yan Yang, James B Murowchick and Bi-Botti C Youan, "Encapsulation of docetaxel in oily core polyester nanocapsules intended for breast cancer therapy." Springer open journal. 2011, 1-12.

[37] Cristina G Venturinia, Eliezer Jagerb, Catiuscia P. Oliveiraa, Andressa Bernardic, Ana M.O. Battastinic, Silvia S. Guterresb, Adriana R. Pohlmanna," Formulation of lipid core nanocapsules." Science-direct.com. 2011, 375, 200-2008.