



Formulation Development and Evaluation of Celecoxib Niosomes

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Abstract

The present study deals with formulation development and evaluation of celecoxib niosomes with main aim of enhancing bioavailability and therapeutic activity over a longer period of time. Niosomes are non-ionic surfactant vesicles obtained on hydration of synthetic nonionic surfactants, with or without incorporation of cholesterol or their lipids. These Niosomes can entrap both hydrophilic and lipophilic drugs and can prolong the circulation of the entrapped drug in body. Encapsulation of drug in vesicular system can predict prolong existence of drug in the systemic circulation and enhance penetration into the target tissue, perhaps reduce toxicity if selective uptake can be achieved. Celecoxib is a NSAID, highly selective cyclooxygenase-2 (COX-2) inhibitor, which is used for treating rheumatoid arthritis, osteoarthritis and acute pain. In the present study celecoxib Niosomes were prepared by thin-film hydration method using different concentrations of Tween 80 or span 80, cholesterol. All the formulation was characterized using differential scanning calorimetry, vesicle size, zeta potential, stability studies, entrapment efficiency. The vesicle size range of celecoxib Niosomes were found to 209-322nm. The invitro release studies revealed that most celecoxib Niosomal formulations released more than 90% of its drug content within 48 hours. Accelerated stability studies were done for about 1month according to ICH guidelines for optimized formulation.

Keywords

Celecoxib, Vesicle size, Zeta potential, Stability studies, Entrapment efficiency.

INTRODUCTION:

The Paul Ehrlich, in 1909, initiated the development for targeted delivery when he is researching a drug delivery mechanism that would target directly to diseased cell. Drug targeting can be defined as the ability to direct a therapeutic agent specifically to desired site of action with little or no interaction with non-target tissue. In niosome, the vesicles forming amphiphile is a non-ionic surfactant such as Span-60 which is usually stabilized by addition of cholesterol and small amount of anionic surfactant such as dicetyl phosphate. The first report of non-ionic surfactant vesicles came from the cosmetic applications devised by L'Oreal. The concept of

incorporating the drug into niosome for a better targeting of the drug at appropriate tissue destination is widely accepted by researchers and academicians. Various types of drug deliveries can be possible using niosomes like targeting, ophthalmic, topical, parental, etc.

Inflammation is a local response of living tissues to injury due to any agent, leads to the accumulation of blood cells and fluids. Arthritis is a diseases characterized by joint inflammation, pain and swelling that lead to permanent joint damage and a loss of flexibility and mobility. Rheumatoid arthritis is the most common inflammatory arthritis that mainly targets the synovial membrane of diarthroidal joints.

An arthritic condition needs a controlled release drug delivery system for a prolonged period for reduction of pain and inflammation and prevention of adverse effects of drugs.

The aim of this work is to formulate, develop, characterize and evaluate niosomes as a drug delivery system for administration of celecoxib to improve its bioavailability and anti-inflammatory efficacy with objectives of decreasing the toxic effects and prolonging its action.

NIOSOMES

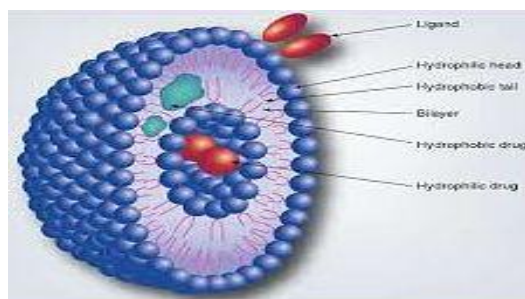
Niosomes are non-ionic surfactant vesicles that are formed from self-assembly of non-ionic amphiphiles in aqueous media resulting in closed bilayer structures. These niosomes are amphiphilic in nature, it allows entrapment of hydrophilic drug in the core cavity and hydrophobic drugs in the non-polar region present within the bilayer. Therefore, both hydrophilic and hydrophobic drugs can be incorporated into niosomes. Niosomes or non-ionic surfactant vesicles are microscopic lamellar structures formed from non-ionic surfactant of the alkyl or dialkyl polyglycerol ether class and

cholesterol with subsequent hydration in aqueous media. In Niosomes, the vesicles forming amphiphile is non-ionic surfactant such as Span 60 which is usually stabilized by addition of cholesterol and small amount of anionic surfactant such as dicetyl-phosphate¹.

Niosomes are one of the best among the carriers. Structurally, niosomes are similar to liposomes and also are equiactive in drug delivery potential but have higher chemical stability and economy makes niosomes superior than liposomes. Both consist of bilayer, which is made up of non-ionic surfactant in the case of niosomes whereas phospholipids in case of liposomes. Niosomes are microscopic lamellar structures of size range between 10 to 1000 nm and consists of biodegradable, biocompatible surfactants.

STRUCTURE OF NIOSOME

A typical niosome vesicle consists of a vesicle forming amphiphile i.e. a non-ionic surfactant such as Span-60, which is usually stabilized by the addition of cholesterol and a small amount of anionic surfactant such as dicetyl phosphate.



COMPOSITIONS OF NIOSOMES

The two major components used for the preparation of niosomes are, Cholesterol, Nonionic surfactants

Cholesterol: Cholesterol provides rigidity and proper shape, conformation to the niosomal preparations.

Nonionic surfactants^{2,3,4}: They play a major role in the formation of niosomes.

The following non-ionic surfactants are generally used for the preparation of niosomes. The nonionic surfactants possess a hydrophilic head and a hydrophobic tail which helps in stabilizing the vesicle.

S.NO	TYPE OF NON-IONIC SURFACTANT	EXAMPLE
1	Fatty alcohol	Cetyl alcohol, steryl alcohol, cetosteryl alcohol, oleyl alcohol
2	Ether	Brij, Decyl glucoside, Lauryl glucoside, octyl glucoside, Triton X-100, Nonoxynol-9
3	Esters	Glyceryl laurate, Polysorbates, Spans
4	Block co-polymers	Polaxmers

S.NO	NAME OF THE SURFACTANT	TRADE NAME	HLB VALUES	DENSITY(g/cm ³)
1	Sorbitan mono laurate	Span20	8.6	1.01
2	Sorbitan mono palmitate	Span40	6.7	1.07
3	Sorbitan mono stearate	Span60	4.7	-
4	Sorbitan mono oleate	Span80	4.3	1.01
5	Sorbitan mono trioleate	Span85	1.8	0.956

Charged molecules:

Some charged molecules are added to niosomes to increase stability of niosomes by electrostatic repulsion by preventing coalescence.

Negatively Charged Molecules:

The mostly used negatively charged molecules are diacetyl phosphate (DCP) and phosphotidic acid.

Positively Charged Molecules:

The well-known positively charged molecules used in niosomal preparations are stearylamine (STR) and stearyl pyridinium chloride. These charged molecules are used mainly to prevent aggregation of niosomes.

TYPES OF NIOSOMES

The niosomes are classified as follows, based on the number of bilayer (e.g. MLV, SUV) or based on size. (e.g. LUV, SUV) or based on method of preparation (e.g. REV, DRV). The various types of niosomes are mentioned below:

- i) Multi lamellar vesicles (MLV), (MLV, Size=>0.05 μm)
- ii) Large unilamellar vesicles (LUV), (LUV, Size=>0.10 μm).
- iii) Small unilamellar vesicles (SUV), (SUV, Size=0.025-0.05 μm)

Multi-lamellar vesicles

It consists of a number of bilayer surrounding the aqueous compartment of lipid separately. Multilamellar vesicles are the most widely used niosomes. These vesicles are highly suitable as drug carrier for lipophilic compounds. The size range of these vesicles is between 0.5-10 μm diameter.

Small unilamellar vesicles (suv):

These vesicles are mainly prepared from multilamellar vesicles by sonication method, French press extrusion electrostatic stabilization is inclusion of dicetyl phosphate in 5(6)-carboxyfluorescein (CF) loaded Span 60 based niosomes.

Large unilamellar vesicles (luv):

Niosomes of this type have a higher aqueous/lipid compartment ratio, therefore larger volumes of bio-active materials can be entrapped with in the membrane lipids.

ADVANTAGES OF NIOSOMES^{5,6,7,8}:

- i. Use of niosomes in cosmetics was first done by L'Oreal as they offered the following advantages. The vesicle suspension being water based offers greater patient compliance over oil based systems.
- ii. Since the structure of the niosome offers place to accommodate hydrophilic, lipophilic as well as amphiphilic drug moieties, they can be used for a variety of drugs.
- iii. The characteristics such as size, lamellarity etc. of the vesicle can be varied depending on the requirement.

- iv. The vesicles can act as a depot to release the drug slowly and offer a controlled release.
- v. They are osmotically active and stable.
- vi. They increase the stability of the entrapped drug.
- vii. Handling and storage of surfactants do not require any special conditions.
- viii. Can increase the oral bioavailability of drugs.
- ix. Handling and storage of surfactants requires no special conditions.
- x. Can enhance the skin penetration of drugs.
- xi. They can be used for oral, parenteral as well topical.
- xii. The surfactants are biodegradable, biocompatible, and non-immunogenic.
- xiii. Improve the therapeutic performance of the drug by protecting it from the biological environment and restricting effects to target cells, thereby reducing the clearance of the drug.
- xiv. The niosomal dispersions in an aqueous phase can be emulsified in a non-aqueous phase to control the release rate of the drug and administer normal vesicles.

DISADVANTAGES OF NIOSOMES:

Physical instability
Aggregation
Fusion
Leaking of entrapped drug.
Hydrolysis of encapsulated drugs which limiting the shelf life of the dispersion.

Applications of niosomes

The application of niosomal technology is widely varied and can be used for treat a number of diseases.

General methods of preparation of niosomes

The preparation methods should be chosen according to the use of the niosomes, since the preparation method will influence the number of bilayers, size, size distribution, and entrapment efficiency of the aqueous phase and the membrane permeability of the vesicles.

- i. Ether injection method
- ii. Hand shaking method (thin film hydration technique)
- iii. Sonication Method
- iv. Micro fluidization Method
- v. Multiple membrane extrusion method
- vi. Reverse Phase Evaporation Technique (REV)
- vii. Trans membranes pH gradient (inside acidic) Drug Uptake Process

Ether injection method

In these method niosomes are prepared by slowly introducing a solution of surfactant dissolved in diethyl ether into warm water maintained at 60°C.

The surfactant mixture in ether is injected through 14-gauge needle into an aqueous solution of material. Vaporization of ether leads to formation of single layered vesicles. Depending upon the conditions used the diameter of the vesicle range from 50 to 1000 nm.

Hand shaking method (thin film hydration technique)

In these method vesicles forming ingredients like surfactant and cholesterol are dissolved in a volatile organic solvent like diethyl ether, chloroform or methanol in a round bottom flask. These organic solvent is removed at room temperature (20°C) by using rotary evaporator leaving a thin film of solid mixture deposited on the wall of the flask. These dried surfactant film can be rehydrated with aqueous phase at 0-60°C with gentle agitation. This process forms typical multilamellar niosomes.

Sonication Method

A typical method of production of the vesicles is by sonication of solution as described by Cable. In this method an aliquot of drug solution in buffer is added to the surfactant/cholesterol mixture in a 10-ml glass vial. The mixture is probe sonicated at 60°C for 3 minutes using a sonicator with a titanium probe to yield niosomes.

Micro fluidization Method

Micro fluidization technique is used to prepare unilamellar vesicles of defined size distribution. This method is based on submerged jet principle in which two fluidized streams interact at ultra-high velocities, in precisely defined micro channels within the interaction chamber. The impingement of thin liquid sheet along a common front is arranged such that the energy supplied to the system remains within the area of niosomes formation. These result in greater uniformity, smaller size and better reproducibility niosomes.

Multiple membrane extrusion method

Mixture of surfactant, cholesterol and dicetyl phosphate in chloroform is made into thin film by evaporation. The film is hydrated with aqueous drug polycarbonate membranes, solution and the resultant suspension extruded for up to 8 passages. This is the best method for controlling the size of niosomes.

Reverse Phase Evaporation Technique (REV)

Cholesterol and surfactant (1:1) are dissolved in a mixture of ether and chloroform. An aqueous phase containing drug is added to this and the resulting two phases are sonicated at 4-5°C. To the clear gel formed small amount of phosphate buffered saline (PBS) is added and sonicated. The organic phase is removed at 40°C under low pressure. The resulting viscous niosome suspension is diluted with PBS and

heated on a water bath at 60°C for 10 min to yield niosomes.

Trans membranes pH gradient (inside acidic) Drug Uptake Process or Remote Loading Technique

Surfactant and cholesterol are dissolved in chloroform. The solvent is then evaporated under reduced pressure to get a thin film on the wall of the round bottom flask. The film is hydrated with citric acid (pH 4.00). The multilamellar vesicles are frozen and later sonicated. To this niosomal suspension aqueous solution containing 10 mg/ml of drug is added and vortexed. The pH of the sample is then raised to 7.0-7.2 with 1M disodium phosphate. This mixture is later heated at 60°C for 10 minutes to give niosomes.

Bubble Method

This technique helps in single step preparation of liposomes and niosomes without the use of organic solvents. The bubbling unit generally consists of round-bottomed flask with three necks positioned in water bath to control the temperature. Water-cooled reflux and thermometer is positioned in the first and second neck and nitrogen supply through the third neck. Cholesterol and surfactant are dispersed together in this buffer (pH 7.4) at 70°C, the dispersion mixed for 15 seconds with high shear homogenizer and immediately afterwards "bubbled" at 70°C using nitrogen gas. The removal of untrapped solute from the vesicles can be accomplished by various techniques like dialysis, gel filtration and centrifugation.

Factors affecting niosomes formulation

1. Drug
2. Amount and type of surfactant
3. Cholesterol content and charge
4. Resistance to osmotic stress

Drug

Entrapment of drug in niosomes increases vesicle size, probably by interaction of solute with surfactant head groups, increasing the charge and mutual repulsion of the surfactant bilayers, thereby increases vesicle size.

Amount and type of surfactant

The mean size of niosomes increases proportionally with increase in the HLB surfactants like Span 85 (HLB 1.8) to Span 20 (HLB 8.6) because the surface free energy decreases with an increase in hydrophobicity of surfactant.

Cholesterol content and charge

Inclusion of cholesterol in niosomes increased its hydrodynamic diameter and entrapment efficiency.

Resistance to osmotic stress

Addition of a hypertonic salt solution to a suspension of niosomes brings about reduction in diameter. In hypotonic salt solution, there is initially slow release

with slight swelling of vesicles occurs due to inhibition of eluting fluid from vesicles, followed by faster release, which may be due to mechanical loosening of vesicles structure under osmotic stress.

MATERIALS AND METHODS:

Materials:

Celecoxib was generous gift from kekule Pharma Ltd (Hyderabad, India), cholesteryl hemi succinate was a kind gift from sigma life sciences. Chloroform was a kind gift from research fine lab. Tween 80 was a kind gift from Finar. Span 80 was obtained from lobachemie and methanol was obtained from research lab fine chem industry.

Analytical Method development for celecoxib

Before the formulation development and evaluation of celecoxib niosomes, standard graph of celecoxib in different media was obtained to quantify the samples. All the solutions were freshly prepared before use.

Preparation of standard stock solution of celecoxib

Accurately weighed 100mg of celecoxib was placed in volumetric flask. The volume was made up to 100ml using methanol to give 1000ppm solution.

Preparation of concentration of Analytical range

The working standard solution of the drug is prepared by pipetting out 1ml of the solution into 10 ml of the volumetric flask and made up to the volume with methanol. (100ppm). Then respective volumes of solutions are pipetted out from the 100ppm solution into 10ml vol flasks to obtain 2,4,6,8,10 ppm of Celecoxib.

Determination of absorption maxima (λ_{max}) for Celecoxib

The above prepared standard solutions of Celecoxib were scanned on double beam spectrophotometer against respective media blanks. An absorption maximum λ_{max}

Of 252nm was obtained for all the solutions. A wavelength of 252nm was selected to prepare standard curve.

Preparation of standard curve for Celecoxib

Standard curves for celecoxib were obtained in 7.4 pH buffers. Aliquots of 2,4,6,8,10ml of Celecoxib

standard solution of 100pp was taken and diluted to obtain appropriate concentration. The absorbance of solution was determined at 252 nm against media as blank. The experiment was repeated six times for each buffer and calibration curve was determined from the mean value.

Solubility studies

The solubility of Celecoxib was determined in various surfactants. The excess amount of drug was added to 1gm of each excipient in different cap vials. The mixture is cyclomixed immediately using cyclo-mixer to increase drug solubilisation. Then the mixtures are placed for heating at 40-50°C for five min. The resultant mixture was then left for equilibration at room temperature on a rotary shaker at a speed of 100rpm for 72 hours. The supersaturated solutions were then centrifuged at a speed of 3000rpm for 15 minutes to remove the undissolved drug. The supernatant was separated and adequately diluted with methanol and concentration of Celecoxib in each excipient was determined spectrophotometrically at λ_{max} 252 nm.

Formulation development and evaluation of Celecoxib niosomes

Formulation development

Niosomes containing Celecoxib were prepared by the thin-film hydration method. Two types of nonionic surfactants were used for the preparation of celecoxib niosomes, namely; Tween 80 and Span 80, Cholesterol (CHOL). All celecoxib niosomal formulations prepared were illustrated.

A mixture of either Tween 80 or Span 80, CHOL was weighted according to the molar ratios investigated, then accurately weighed 20 mg of celecoxib was added to the lipid mixture. All ingredients were dissolved in 10 ml chloroform and then the organic solvent was removed by rotary evaporation under reduced pressure, on a water bath at $60 \pm 2^\circ\text{C}$. The deposited lipid film was then hydrated with 10 ml of phosphate buffer of pH 7.4 by rotation in a water bath, at $60 \pm 2^\circ\text{C}$ for 45 min.

Formulation table:

Table no.1: Composition of the prepared Celecoxib niosomeal formulation

Ingredients (Molar ratio)	F ₁	F ₂	F ₃	F ₄
Cholesterol	1	1	1	1
Tween 80	—	1	2	—
Span 80	1	—	—	2
Chloroform	10 ml	10ml	10ml	10ml

Evaluation of celecoxib niosomes

Zeta-potential and Vesicle Size Determinations:

Niosomal zeta-potential and vesicle size for the prepared celecoxib niosomes were determined using dynamic light scattering (DLS) based on laser diffraction at room temperature by Zeta Potential/Particle Sizer equipped with a 5 mW laser with a wavelength output of 632.8 nm and a scattering angle of 90.0°, which is capable of measuring vesicles in 1 nm - 5µm size range.

At investigation time, all niosomal suspensions were diluted with de-ionized water (1:100 v/v). The polydispersity index (P.I.) was determined as an indication of homogeneity.

(P.I.) = Standard deviation/ Mean droplet size

Entrapment Efficiency for Celecoxib: The free celecoxib was separated from the niosome-intercalated celecoxib by cooling centrifugation adjusted to $5200 \times g$ at -4°C using the refrigerated centrifuge. The niosomal pellets were then washed once. The washed pellets were resuspended in 10 ml normal saline and the amount of celecoxib entrapped in niosomes was determined by lysis of 1 ml of resuspended pellets with 50 ml methanol followed by ultra-sonication in the bath-type ultrasonicator for 30 min⁸, then the solution was

double filtered with micro pore filter (pore size 0.2 µm) to discard any niosomal particles may be suspended in the solution. A clear solution was obtained which was measured spectrophotometrically at 252 nm against drug-free niosomes, prepared by the same way, as a blank.

Entrapment efficiency (EE %) = (amount of drug entrapped/ total amount of drug added) \times 100.

In-vitro release Profiles of Celecoxib Niosomes:

This study was conducted on celecoxib niosomal formulations, namely; F₁, F₂, F₃, F₄ celecoxib niosomes. A one ml sample from each niosomal suspensions was transferred to a cellophane membrane, molecular weight cut off 12000 – 14000, immersed in a beaker containing 100 ml PBS (pH 5.5) containing 40% methanol, based on solubility characteristic of the drug¹⁰, to fulfill sink condition. The beaker was placed in a water bath shaker to maintain the temperature at $32 \pm 2^{\circ}\text{C}$, with gentle agitation. At predetermined time intervals (1, 2, 3, 4, 6, 8, 24 and 48 h); 4 ml of the release medium were withdrawn for analysis and replaced with an equal volume of fresh PBS (pH 7.4) containing 40% methanol at $32 \pm 2^{\circ}\text{C}$ to maintain a constant volume. The absorbance of the collected samples was measured spectrophotometrically.

RESULTS AND DISCUSSION:

Preformulation studies

API Evaluation

a) Organoleptic Evaluation

Table No.2: Organoleptic properties of Celecoxib

Properties	Results
Description	powder
Taste	Tasteless
Odour	Odourless
Colour	White

b) Solubility

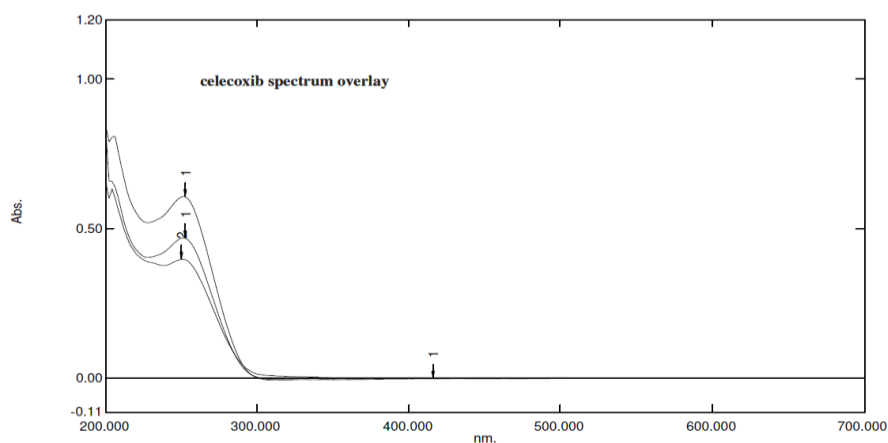
Celecoxib practically insoluble in water and ethanol, soluble in chloroform, methanol, acetone, Dimethyl sulfoxide (DMSO).

Determination of λ_{max} of Celecoxib

From the U.V spectrophotometric analysis it was concluded that the drug, celecoxib showed a λ_{max}

at 252 nm which was similar with the report λ_{max} of Celecoxib (USP). Therefore, the observed λ_{max} was used for further experimental work to analyze the test samples

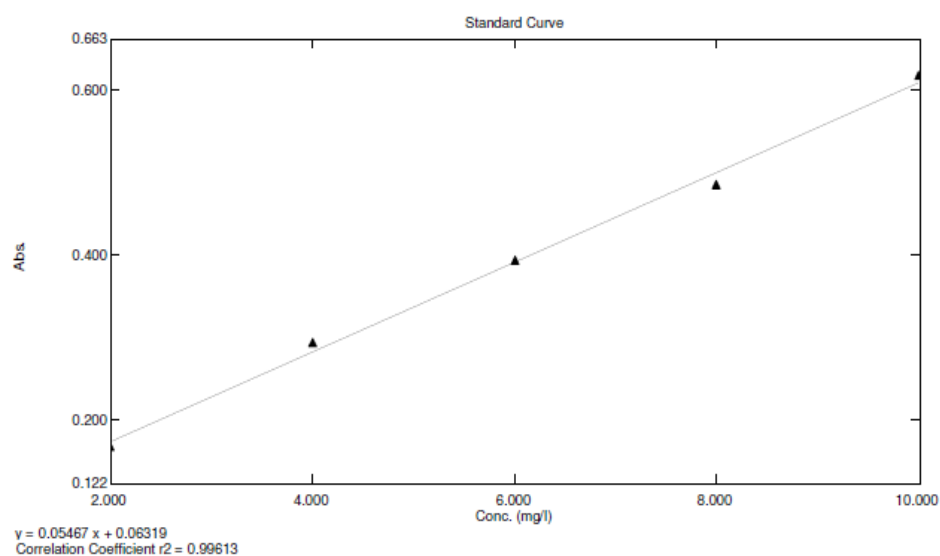
Determination of λ_{\max} of Celecoxib in Methanol



celecoxib 6ppm_151422 - RawData
celecoxib 8ppm_151632 - RawData
celecoxib 10ppm_151826 - RawData

Table no.3: Standard graph of Celecoxib in methanol

Concentration	Absorbance
2	0.167
4	0.293
6	0.393
8	0.485
10	0.618



8.1.2 Standard graph of Celecoxib in pH 7.4 buffer

The concentrations of Celecoxib and the corresponding absorbance's were given in table and plot of concentration versus absorbance was shown. The solution obeyed Beer-Lamberts law over a

concentration range. With regression co-efficient of 0.996. This standard curve was used further to estimate Celecoxib in the invitro samples.

Determination of λ_{\max} of Celecoxib in pH7.4 buffer

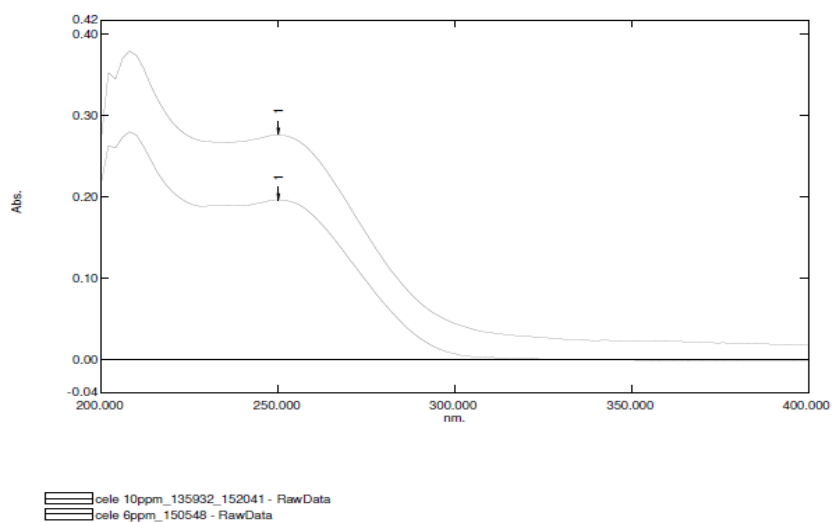
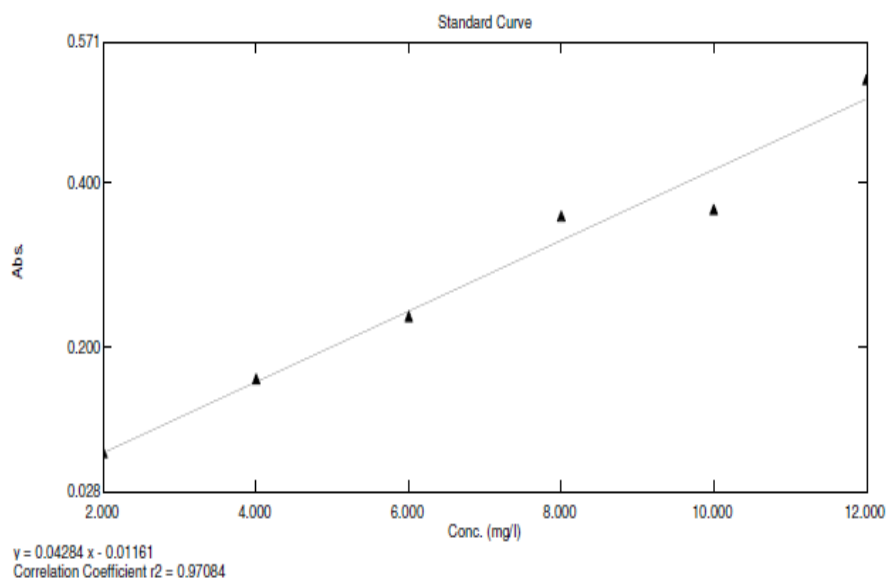


Table no.4: Standard graph of Celecoxib in pH 7.4 buffer

Concentration	Absorbance
2	0.073
4	0.164
6	0.239
8	0.360
10	0.368
12	0.526

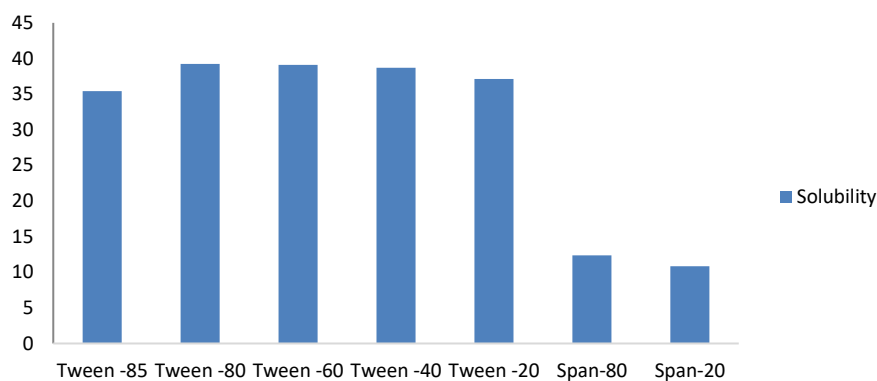


Solubility of Celecoxib In Surfactants



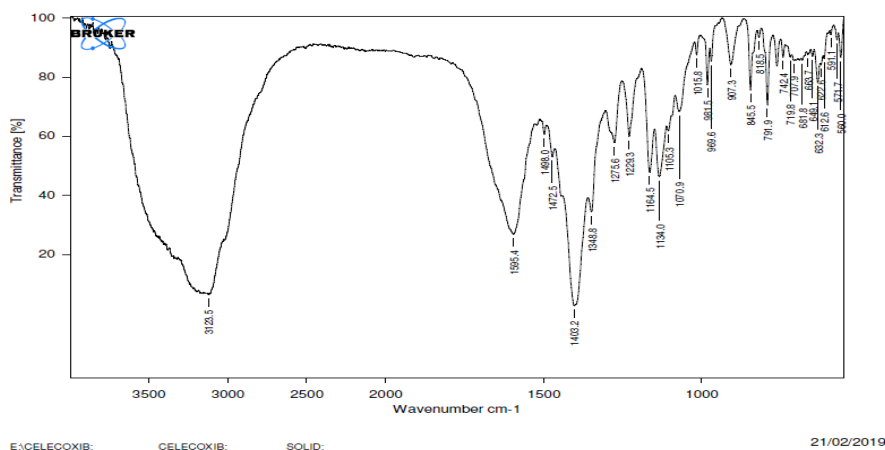
Surfactants	Solubility
Tween -85	35.41mg/ml
Tween -80	39.24 mg/ml
Tween -60	39.08 mg/ml
Tween -40	38.68 mg/ml
Tween -20	37.11 mg/ml
Span-80	12.35mg/ml
Span-20	10.85mg/ml

Solubility of Celecoxib in Surfactants (mg/ml)

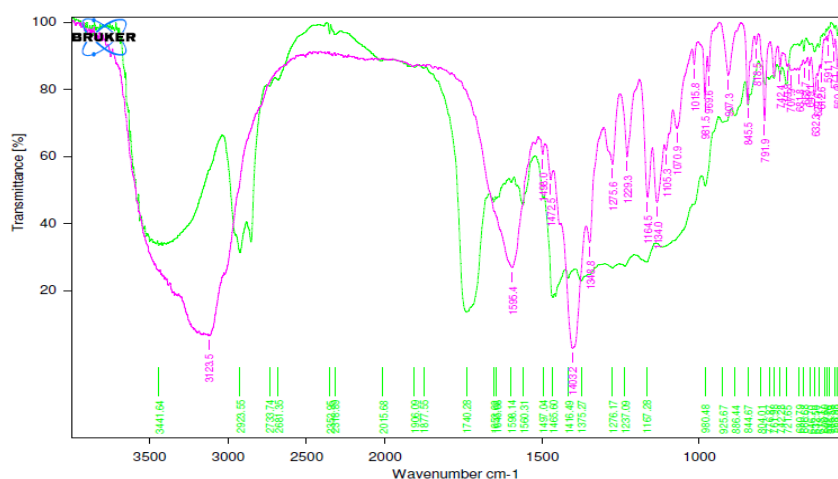


Based on solubility studies, Celecoxib possessed maximum solubility in Tween 80, Tween 60 as surfactants.

Fourier-Transform Infrared (FTIR) Study Celecoxib Pure Drug FTIR Spectra



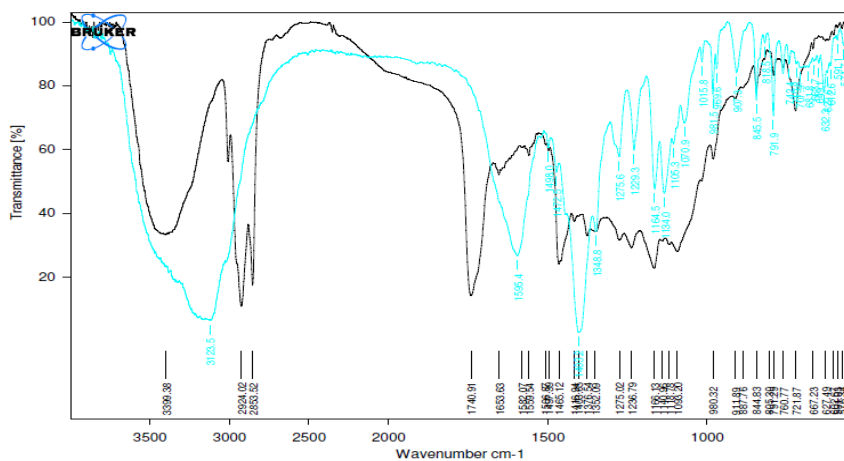
Celecoxib and Span 20



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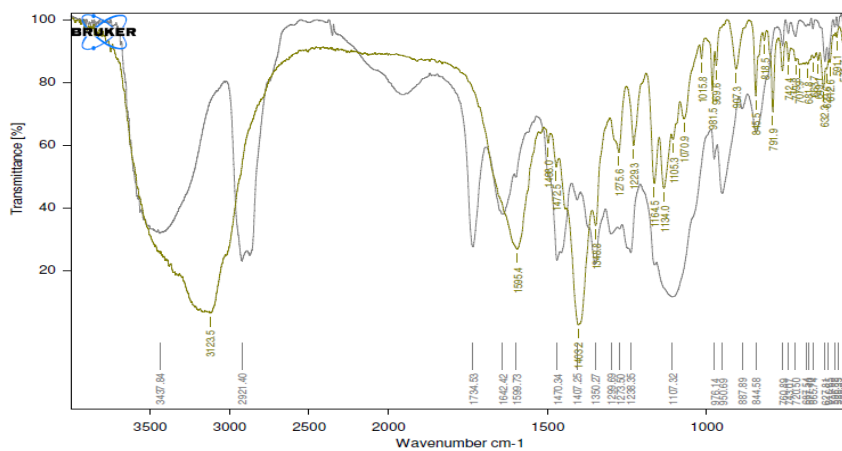
Celecoxib and Span 80



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6	6	6
7	7	7
8	8	8
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99	99	99
100	100	100

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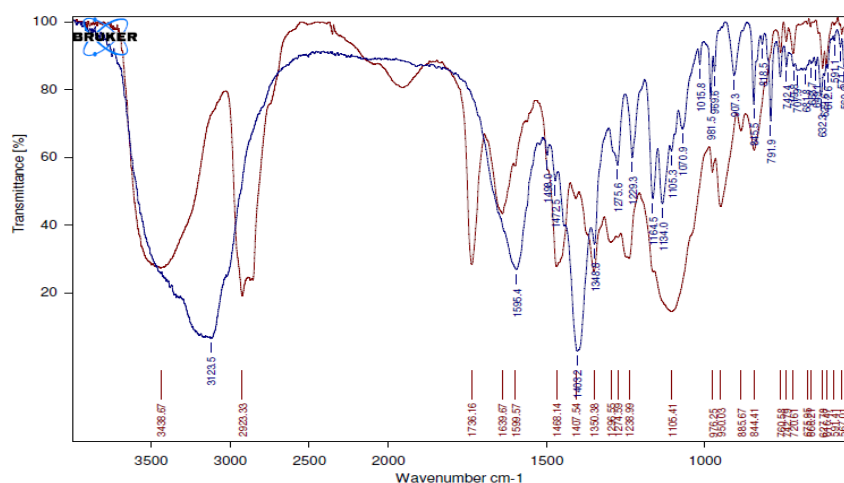
Celecoxib and Tween 20



Formulation	CELECOXIB:	CELECOXIB:	SOLID:
1	100.00	100.00	100.00
2	100.00	100.00	100.00
3	100.00	100.00	100.00
4	100.00	100.00	100.00
5	100.00	100.00	100.00
6	100.00	100.00	100.00
7	100.00	100.00	100.00
8	100.00	100.00	100.00
9	100.00	100.00	100.00
10	100.00	100.00	100.00
11	100.00	100.00	100.00
12	100.00	100.00	100.00
13	100.00	100.00	100.00
14	100.00	100.00	100.00
15	100.00	100.00	100.00
16	100.00	100.00	100.00
17	100.00	100.00	100.00
18	100.00	100.00	100.00
19	100.00	100.00	100.00
20	100.00	100.00	100.00
21	100.00	100.00	100.00
22	100.00	100.00	100.00
23	100.00	100.00	100.00
24	100.00	100.00	100.00
25	100.00	100.00	100.00
26	100.00	100.00	100.00
27	100.00	100.00	100.00
28	100.00	100.00	100.00
29	100.00	100.00	100.00
30	100.00	100.00	100.00
31	100.00	100.00	100.00
32	100.00	100.00	100.00
33	100.00	100.00	100.00
34	100.00	100.00	100.00
35	100.00	100.00	100.00
36	100.00	100.00	100.00
37	100.00	100.00	100.00
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72	100.00	100.00	100.00
73	100.00	100.00	100.00
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75	100.00	100.00	100.00
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78	100.00	100.00	100.00
79	100.00	100.00	100.00
80	100		

21/02/2019

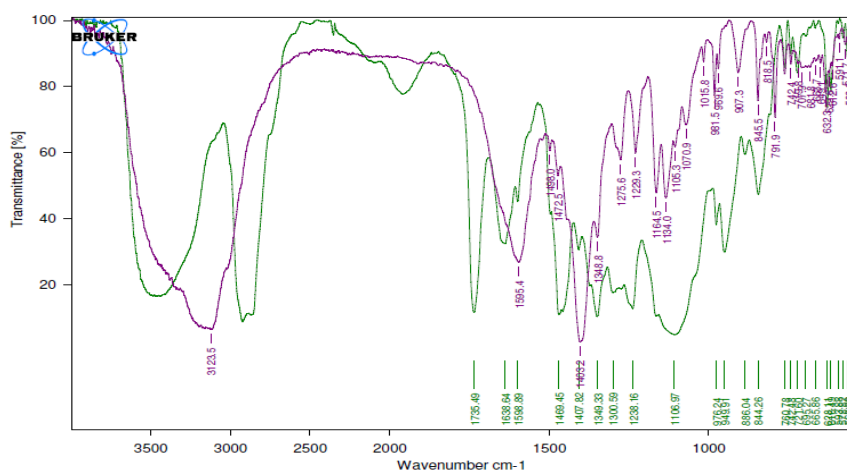
Celecoxib and Tween 40



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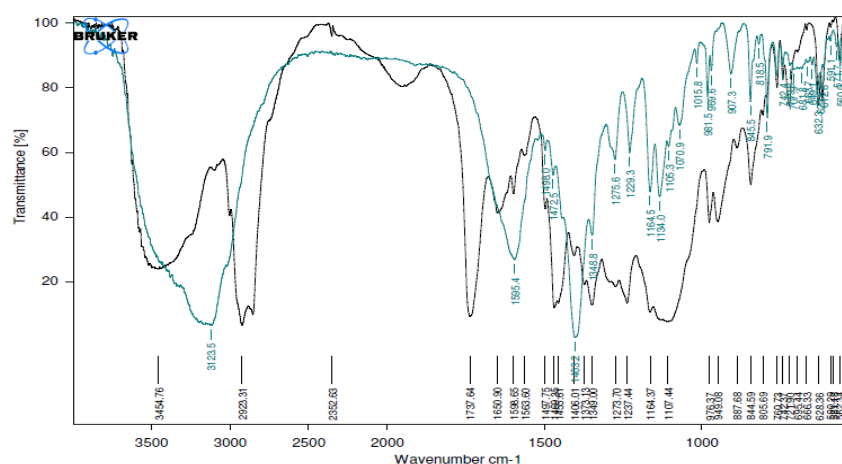
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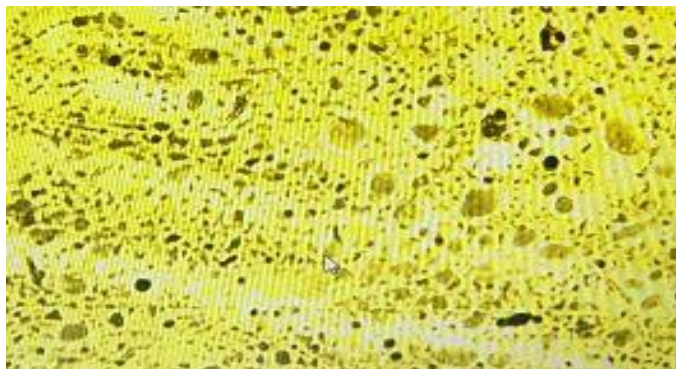
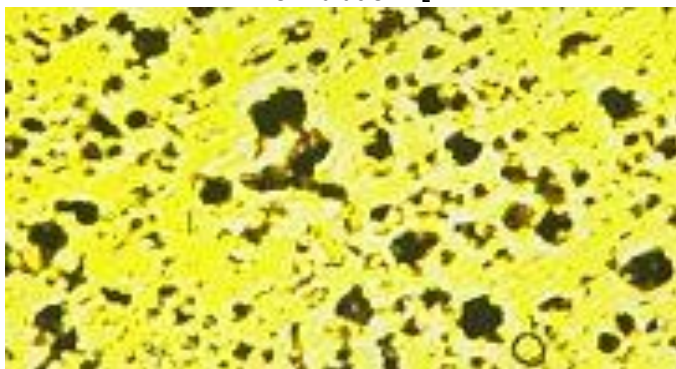
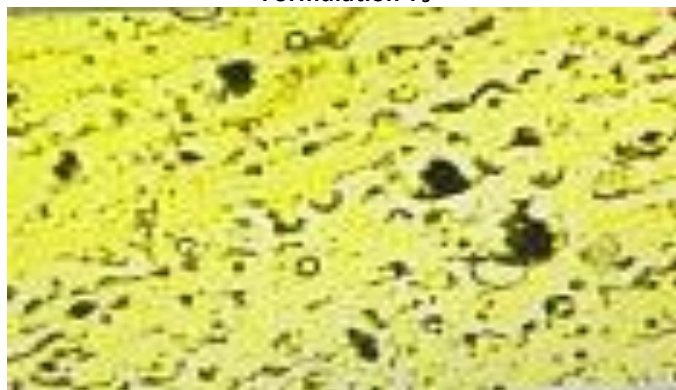
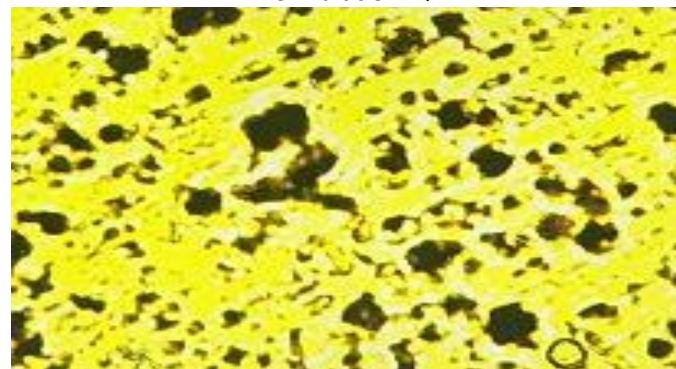
21/02/2019

Celecoxib and Tween 85



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CELECOXIB NIOSOMAL FORMULATIONS (FLOUROSCENT MICROSCOPY):**Formulation-F₁****Formulation-F₂****Formulation-F₃****Formulation-F₄**

Evaluation of Celecoxib Niosomes

Drug content:

Formulation	Drug content
F1	89.02±0.23%
F2	95.14±0.32%
F3	97.27±0.17%
F4	85.57± 0.46%

Zeta-potential and Vesicle Size Determinations:

Of all the Formulations F3 was found to be optimized.

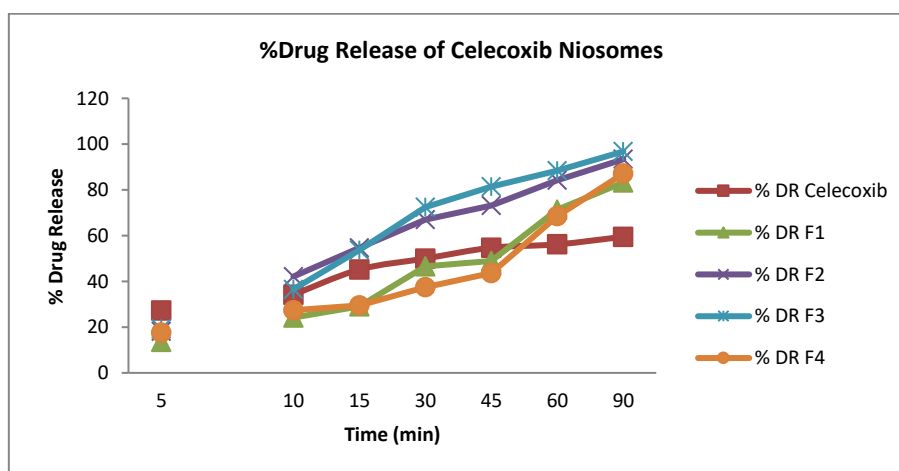
Formulation	Vesicle size(nm)	PDI	Zeta potential (mV)
1	243.7	0.351	-20.3
2	360.4	0.236	-23.1
3	209.3	0.272	-19.6
4	420.3	0.277	-31.1

Entrapment Efficiency for Celecoxib:

Formulation	Entrapment Efficiency
F1	87.18±0.35%
F2	92.31±0.28%
F3	98.40±0.37%
F4	84.92±0.52%

In-vitro release Profiles of Celecoxib Niosomes:

Time (min)	%Drug released (Celecoxib)	%Drug released F1	%Drug released F2	%Drug released F3	%Drug released F4
5	27.21	13.56±0.12	18.20±0.01	19.30±0.11	17.55±0.05
10	34.14	24.17±0.17	42.12±0.12	36.54±0.15	27.4±0.05
15	45.18	29.13±0.07	54.72±0.21	53.75±0.17	29.49±0.01
30	49.98	46.55±0.08	67±0.15	72.39±0.16	37.46±0.04
45	54.69	48.88±0.15	73.09±0.31	81.34±0.13	43.57±3.06
60	56.17	71.30±0.18	84.22±0.11	88.36±0.34	68.57±0.06
90	59.48	83.22±0.04	93.37±0.24	96.78±0.12	87.11±0.16



SUMMARY AND CONCLUSION:

Rationale of the present study was to enhance bioavailability and improve anti-inflammatory efficacy of the drug in the form of niosomes.

Attempt has been made for formulation of celecoxib niosomes, these niosomes are used for treating rheumatoid arthritis, osteoarthritis and acute pain. The celecoxib niosomes were prepared by thin film

hydration method using different concentrations of Tween 80 or span 80, cholesterol and evaluated for parameters like Drug content, Zeta-potential and Vesicle Size Determinations, Entrapment Efficiency, *In-vitro* release.

From the above study all the formulation showed good entrapment efficiencies ranged from 84.92 to 98.40% but the niosomal formulation F₃ prepared from cholesterol and tween 80 (1:2) exhibited the highest percentage of entrapment efficiency while the niosomes prepared from cholesterol and span 80 (1:2) formulation F₄ showed least entrapment efficiency. Zeta potential reveals that niosomal formulation F₃ prepared from cholesterol and tween 80 (1:2) have good stability. Vesicle size determination depicted that the size of celecoxib niosomal formulation ranged from 209.3 to 420.3nm, while the vesicle size of niosomal formulation F₃ is 209.3nm. *In vitro* Drug release study reveals that formulation F₃ prepared from cholesterol and tween 80 (1:2) showed 96% drug release. Therefore, it is concluded that niosomal formulation F₃ exhibited good entrapment efficiency, zeta potential, maximum drug release that leads to enhancement of bioavailability and improves the anti-inflammatory efficacy of celecoxib.

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