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Research Paper -Pharmaceutical Science

Formulation and Evaluation of Enteric Coated Tablets of Diclofenac Sodium Using Hp-55 & Colorcoat Ec4w

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A B S T R A C T

Diclofenac Sodium is used in Inflammatory disorder may include musculoskeletal complaints, especially arthritis, rheumatoid arthritis,, osteoarthritis, dental pain, gout attacks, and pain management in cases of kidney stones and gallstones. An additional indication is the treatment of acute migraines. Diclofenac Sodium is used commonly to treat mild to moderate post-operative or post-traumatic pain, in particular when inflammation is also present, and is effective against menstrual pain and endometriosis.

Diclofenac Sodium is associated with upper gastrointestinal (GI) tract side effects including a high incidence of gastric and duodenal ulceration. Hence the present work was undertaken to formulate enteric coated tablets of Diclofenac sodium with an objective:

* ***To prevent the side effect associated with the upper gastrointestinal (GI) Tract i.e high incidence of gastric and duodenal ulceration.***
* ***To improve therapeutic efficacy of drug through modified release dosage forms such as Enteric coating(EC) or sustain release(SR) formulation.***
* ***Method by which delayed release is achieved can improve the bioavailability of some drugs e.g drugs susceptible to acid pH can be protected by enteric coating in polymer systems suitable for delayed release.***

Introduction

Oral administration of drugs has been the most common and preferred route for delivery of most therapeutic agents. The popularity of the oral route is attributed to patient acceptance and ease of administration. In oral drug delivery system, there are many types of dosage forms available to deliver the drugs such as tablets, capsules, liquids etc. However, tablet dosage forms are preferred due to their accurate dose, good physical and chemical stability, competitive unit production costs and an elegant distinctive appearance resulting in a high level of patient acceptability.

Orally administered drug must be absorbed through the gut which depends on various factors such as gastric emptying, intestinal motility, mucosal surface area, degradation of drug in the stomach and first pass effect. The absorption rate varies from the stomach to the intestine owing to the increased surface area (about 4500 cm2), the intestinal mucosa and greater blood flow (1000 ml/min) through the intestinal capillaries compared to the gastric capillaries. It is also known that some drugs possessing pH dependent stability which are not stable in acidic environment (in the stomach). Various techniques have been developed to overcome this stability problem. One out of them is development of enteric coated products. These enteric-coated dosage forms resist the acidic environment of the stomach and allow disintegration in the higher pH environment of the intestinal fluid. The enteric coating on a solid dosage form can also be used for site-specific drug delivery of a therapeutic agent to the intestinal region.

Enteric coating:

The technique involved in enteric coating is protection of the tablet core from disintegration in the acidic environment of the stomach by employing pH sensitive polymer, which swell or solubilize in response to an increase in pH to release the drug.

Reasons for enteric coating:

1) To prevent degradation of acid sensitive active pharmaceutical ingredient.
2) To prevent irritation of stomach by certain drugs like sodium salicylate. iii) Delivery of active pharmaceutical ingredient into intestine.
3) To provide a delayed release component for repeat action tablet.

Ideal properties of enteric coating material: -

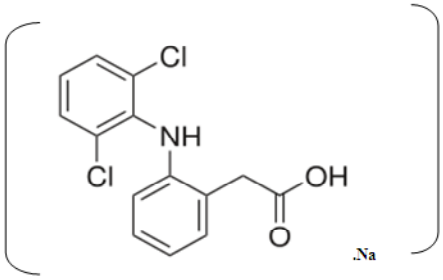
- Resistance to gastric fluids.
- Susceptible/permeable to intestinal fluid.
- Compatibility with most coating solution components and the drug substrate.
- Formation of continuous film.
- Nontoxic cost effective and ease of application.
- Ability to be readily printed.

Drug Profile

Diclofenac Sodium

IUPAC Name: sodium 2- [(2,6-dichlorophenyl)amino]phenylacetate

Molecular formula: $C_{14}H_{11}Cl_2NO_2$ Na
Molecular weight: 318.13
Structure: .Na



Description

Diclofenac sodium is an odorless, yellowish-white, crystalline powder sparingly soluble in water.

Bioavailability

60% (young healthy subjects), 65% (elderly); 85% (patients with cancer) and 100% (severe hepatic impairment).

Half-life

1.2-2 hr (35% of the drug enters enterohepatic recirculation

Volume of distribution

The apparent volume of distribution calculated is 0.12 to 0.17 L/kg.

Clearance

biliary, only 1% in urine

Distribution in blood

99.7% of diclofenac is bound to serum proteins, mainly to albumin (99.4%).

Dose

Adult: 25 mg, 50mg (orally)

Mechanism of action

The exact mechanism of action is not entirely known, but the primary mechanism responsible for its anti-inflammatory, antipyretic, and analgesic action is thought to be inhibition of prostaglandin synthesis by inhibition of cyclooxygenase (COX). It also appears to exhibit bacteriostatic activity by inhibiting bacterial DNA synthesis.

Material Required

1) Sodium Starch Glycolate

Chemical Name:- Sodium carboxy methyl starch..

Functional Category:- Tablet and capsule disintegrant.

2) Magnesium Stearate

Chemical Name:- Octadecanoic acid magnesium salt.

Functional Category:- Tablet and capsule lubricant.

3) Micro Crystalline Cellulose

Chemical Name:- Cellulose..

Functional Category:- Adsorbent, Suspending agent, Tablet & Capsule diluents, Tablet disintegrant

4) Hydroxy Propyl Methyl Cellulose- P

Chemical Name- Cellulose, Hydrogen 1,2- benzenedi carboxylate, 2-hydroxypropyl, Methyl ether.

Functional Category- Coating agent.

5) Isopropyl Alcohol

Chemical Name- Propan-2-ol..

Functional Category- Disinfectant, solvent.

6) Poly Vinyl Pyrrolidine

Chemical Name- Poly[1-(2-oxo-1-pyrrolidinyl)ethylen] 1-Ethenyl-2-pyrrolidon homopolymer 1-Vinyl-2-pyrrolidinon-Polymere Copovidone

Functional Category- Used as a binder.

7) Starch

Functional Category- Pharmaceutical aid (filler, binder, disintegrant); dusting powder.

8)Talc

Chemical Name- Hydrated magnesium silicate.

Functional Category- it is used as lubricating agent

9) Titanium Dioxide

Chemical Name- Titanium dioxide.

Functional Category- As a plasticizers

11) Sunset Yellow Lake

Chemical Name- Disodium 6-hydroxy-5-[(4-sulfophenyl)azo]-2-naphthalenesulfonate

Functional Category- Colouring agent.

12) Methylene Di Chloride

Chemical Name- Dichloromethane

Functional Category- Used as a solvent.

Evaluation Of Diclofenac Sodium (50 Mg) Coated Tablets:-

Pre Compression Parameters:-

Average weight
Thickness
Weight variation
Hardness
Friability
Disintegration test
Dissolution test

Result And Discussion

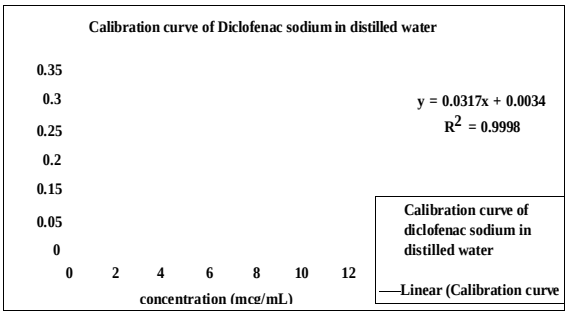
Standard Calibration Curve For Diclofenac Sodium In Distilled Water:

UV Spectrophotometer method

Table No. 1

S.no	Concentration (Mcg/Ml)	Absorbance
1)	2	0.066
2)	4	0.130
3)	6	0.196
4)	8	0.256
5)	10	0.32

Figure no.1



Standard Calibration Curve For Diclofenac Sodium In Phophate Buffer:

Table No.2

S.no	Concentration (Mcg/Ml)	Absorbance
1)	2	0.067
2)	4	0.137
3)	6	0.194
4)	8	0.260
5)	10	0.323

Post Compression Parameters (Core Tablet)

Physical properties of tablet formulation:-

S.N	Physical Properties	F1	F2
1)	Average weight (mg)	144.50 mg	142.35 mg
2)	Hardness (kg/cm2)	5.0 kg/cm2	5.5 kg/cm2
3)	Friability (%)	0.205 %	0.139%
4)	Thickness (mm)	2.8 mm	3.0 mm
5)	Disintegration test (min)	5.36 min	5.0 min

Each volume is the mean ± SD (n=3)

Physical properties of enteric coated formulation:-

S.N.	PARAMETERS	F1	F2
1)	Thickness (mm)	3.0 ± 0.5 mm	3.5 ± 0.5 mm
2)	Disintegration test (0.1N Hcl) (min)	Stable	stable
3)	Disintegration test phosphate(buffer pH 6.8)(min)	20min	25min

Assay of the drug content:-

The assay of diclofenac sodium is performed by U.V spectophotometry and the result are given in table below:

In Vitro Dissolution Studies:-

TABLE:-

S.no	Parameters	F1	F2
1)	Drug content	100.42%	101.23%

Table:- In vitro dissolution studies.

S.no	Time Point	F1	F2
1)	2hours (0.1N Hcl)	2.13 ± 0.25	2.4 ± 0.1
2)	5 min (buffer pH6.8)	3.95 ± 0.28	2.4 ± 0.1
3)	10 min	4.31 ± 0.43	2.4 ± 0.1
4)	15 min	13.06 ± 0.33	24.1 ± 0.15
5)	20min	71.53 ± 0.82	35.1 ± 0.02
6)	30min	92.19 ± 0.37	78.4 ± 0.045
7)	45 min	95.13 ± 0.7	92.3 ± 0.045

See Table 1

Discussion

Site specific, Drug delivery of a therapeutic agent to the intestinal region can be readily accomplished by the application of an enteric coating on a solid dosage form . enteric coatings have been used for many years to arrest the release of the drug from the orally ingestible dosage form. Depending upon the composition and thickness, the enteric coatings are resistant to stomach acid for required period of time before they begin to disintegrate and permit release of the drug in the lower stomach and or upper part of the small intestine. Diclofenac sodium is a inhibitor of prostaglandin synthesis by inhibition of cyclooxygenase (cox). Diclofenac sodium causes gastric ulcer on continuous use for long time. But the therapeutic activity of the drug is good so in order to eliminate the G.I ulcer by drug, delayed release- enteric coated product developed.

Conclusion

In the present study, Diclofenac enteric coated tablets were prepared using enteric coating polymer like Hydroxyl Propyl Methyl Cellulose- Phthalate, Colorcoat EC4W. From this study it can be concluded that Diclofenac sodium enteric coated tablets prepared by Hydroxy Propyl Methyl Cellulose- Phthalate and Poly Ethylene Glycol is good and cost effective than readymix colorcoat EC4W. The two formulations with 10-12% weight gain was consider optimum because it showed negligible drug release in acidic medium and drug release in the phosphate buffer (PH6.8) was found to be almost complete.

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