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Research

Formulation development and evaluation of Mini-Tablets in Enteric Capsule Drug Delivery Technology of Diclofenac sodium

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Abstract

Enteric capsule drug delivery technology (ECDDT) was developed to allow for fast GI tract release without coating and full enteric protection during oral route of administration Enteric capsule drug delivery technology eliminated the need for enteric coatings preparations and application process which means that development time can be shorter and program risk can be lower. Pellets that are easy to make have low porosity and all the same size and shape have smooth surface and don't change from batch to batch can be turn into mini tablets which another to way to take medicine, the current study aimed to create a mini tablet within the Enteric capsule drug delivery technology considering the advantage of Enteric capsule drug delivery technology and mini tablets the Diclofenac sodium served as a model drug to elucidate the drug release profile and drug kinetics and stability assessment.

Keywords: Formulation, Development, Evaluation, ECDDT, Diclofenac sodium

INTRODUCTION

Enteric Capsule Drug Delivery Technology ECDDT was created, where pharmaceutically approved enteric polymers are incorporated into the capsule shell to provide acid resistance without another coating. This review article describes several commercially available hard capsules prepared by the ECDDT method and their properties.

Enteric Capsule Drug Delivery Technology: Enteric capsule drug delivery technology ECDDT was developed to provide oral delivery with full enteric protection and rapid release in the upper gastrointestinal GI tract without the use of coatings. ECDDT's intrinsically enteric properties are attained by incorporating pharmaceutically approved

enteric polymers in the capsule shell using conventional pin-dipping capsule manufacturing processes. By eliminating the preparation and application steps used for enteric coating, ECDDT can offer accelerated development timelines and reduced program risk. ECDDT can also enable the oral delivery of sensitive molecules, such as nucleotides and peptides, biological products such as vaccines, and live bio therapeutic products LBPs, which can degrade at the high temperatures or can be sensitive to aqueous coating solution associated with pan and fluid bed coating processes. The enteric properties and rapid release of specialized ECDDT capsule shells have been demonstrated to meet pharmacopeia standards for both in vitro and in vivo performance using esomeprazole magnesium trihydrate EMT as a model compound.

Mini-Tablets: Pharmaceutical mini-tablets are novel solid dosage forms that can be as small as 1 mm in diameter. Mini-tablets with a size of around 2.5 mm meet the Food and Drug Administration guidance for industry "Size of beads in drug products labelled for sprinkle," Rev. 1, published in May 2012.

Mini-tablets combine the advantage of both solid and liquid formulations. Mini-tablets are viable options that can be successfully adopted for pediatrics and geriatric populations.

Manufacturing: Mini-tablets are manufactured using standard rotary tablet presses. However, minor modifications to the press or to the instrumentation may be needed. Manufacture of mini-tablets will require special tooling, which is generally more expensive when compared to the tooling used in the manufacture of normal tablets. All major tooling companies supply what is called stepped tooling, where punches have shorter stems to reinforce the tooling tip strength and reduce the risk of potential damage to the punches.

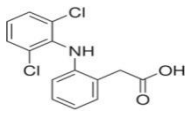
Methods of manufacturing mini-Tablets:Direct compression Dry granulation Wet granulation Melt extrusion The manufacturing process typically involves unit operations such as dry or wet granulation to improve flow properties, compression using multiple tooling, Wurster or pan coating, and encapsulation or stick packing. These manufacturing processes have a number of technological challenges when producing mini- tablets when compared to conventional tablets, but careful evaluation of each unit operation can produce a better-suited and more robust mini- tablet-based dosage form. As such, mini-tablets seem best implemented for small-volume, high- value products, particularly for paediatric patient populations that would benefit from this unique dosage form.

Materials and Methods:

Materials: Diclofenac Sodium-SS Pharma Labs, Hyderabad., India, Microcrystalline Cellulose112- Signet Excipients, Bangalore., India, Sodium Starch Glycolate Ash land (Pvt. Ltd), Maharashtra., India, Hydroxy Propyl methyl cellulose- Signet Excipients, Bangalore., India, Magnesium Stearate-SRL Chem (Pvt. Ltd), Maharashtra., India, Talc- SRL Chem (Pvt. Ltd), Maharashtra., India, Enteric coated capsules- XPRS Nutra, USA

Equipment/Instrument**:** U.V. Visible spectrophotometer–PG Instruments, FTIR spectrophotometer-Perkin Elmer Spectrum-1, Dissolution test apparatus-Lab India, Digital PH meter- Wensar, Digital weighing balance-LC-GC,Tablet Compression Machine-Kalweka.

DRUG PROFILE: Diclofenac Sodium: Molecular Formula: $C_{14}H_{10}Cl_2NNaO_2$: Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti- inflammatory, analgesic, and antipyretic activities in animal models. The mechanism of action of Diclofenac, like that of other NSAIDs, is not completely understood but may be related to prostaglandin synthetase inhibition.



Excipient Profile**:** Microcrystalline cellulose, Hydroxy Propyl methyl cellulose Sodium starch glycolate,Magnesium stearate Talc

Assessment of enteric coated capsules: Enteric coated capsules were assessed for integrity in demonized water, pH 6.8 phosphate buffer and 0.1N hydrochloric acid for 2 hours.

Methodology for Diclofenac Sodium: Preparation of standard calibration curve: UV spectroscopy method was used for budesonide estimation. A 5-ppm standard solution of Diclofenac sodium in 6.8 pH phosphate buffer solution was scanned on a double beam UV spectrophotometer. From UV spectrum, Diclofenac sodium λ max was obtained. The absorbance of solutions was determined against blank. A standard graph showing the absorbance vs. different concentrations was plotted and correlation coefficient (R^2) was also calculated.

Formulation Development: All the ingredients were weighed according to the quantities specified in Table 3 and passed through #60 meshes separately. Then the ingredients were mixed in geometrical order and compressed into tablets of 50mg by using 8-station rotary mini press tablet machine using 5mm punch. Compressed tablets were filled into Enteric Coated capsule of size#0. Each capsule contains 4 mini-tablets. The dose of each capsule is 25mg.

Diclofenac Sodium Mini-Tablets Formulations:

S.No	Ingredient(mg)	DF1	DF2	DF3	DF4	DF5	DF6	DF7	DF8	DF9
1	Diclofenac	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25	6.25
2	Microcrystalline Cellulose 112	37	19	22	20.5	29.5	26.5	35.5	34	28
3	HPMC K4M	5	20	20	20	12.5	12.5	5	5	12.5
4	Sodium Starch Glycolate	1	4	1	2.5	1	4	2.5	4	2.5
5	Magnesium Stearate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
6	Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Total Tablet Weight (mg)		50	50	50	50	50	50	50	50	50

Pre-compression evaluation of mini-tablets: Bulk density, Tapped density, Angle of repose, Compressibility Index and Hausner's ratio were evaluated according to USP General chapter <1174> to assess the flow property of the blend before compression. Post-compression evaluation of mini-tablets: Compressed tablets were evaluated for post compression parameters according to the procedure mentioned in the following USP general chapters Weight Variation & Drug Content <905> [96], Hardness, Thickness & Friability <1217>. In-Vitro dissolution was performed according to the procedure mentioned in Budesonide USFDA dissolution database. Mini-Tablets encapsulated enteric coated capsules were assessed for maintaining the integrity in 0.1N HCL acidic pH for 2 hours while maintaining dissolution conditions (USP Apparatus Type II; 900mL, 50 RPM; 37°±5°C; followed by (USP Apparatus Type II; 6.8 pH Phosphate Buffer; 900mL, 50RPM; 37°±5°C; 60 Minutes) at sampling intervals of 15, 30, 45 & 60 Minutes). Samples obtained were determined by UV-visible spectrophotometer at 277nm.
Release Kinetics: The drug release kinetics study was conducted on optimized formulation related to various kinetic models, namely, zero-order kinetics, first-order kinetics, Higuchi and Korsmeyer-Peppas models, and then the regression analysis (R^2) and diffusion coefficient
(n) were determined.

Results and Discussion:

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4	SodiumStarch Glycolate	1	4	1	2.5	1	4	2.5	4	2.5
5	Magnesium Stearate	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
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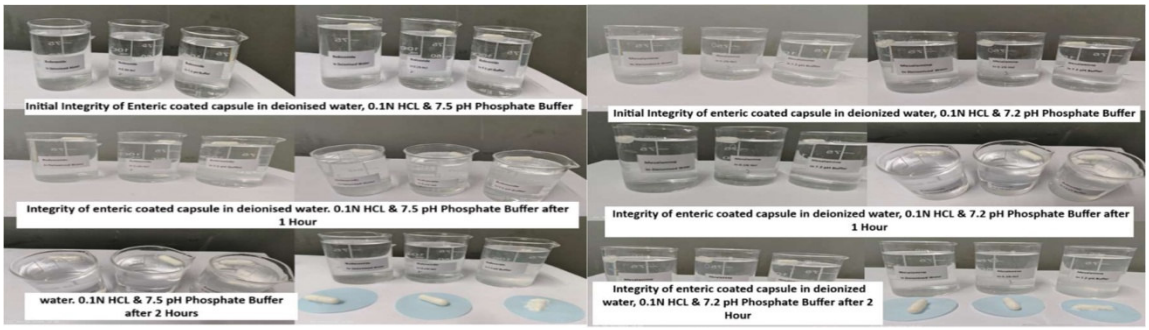
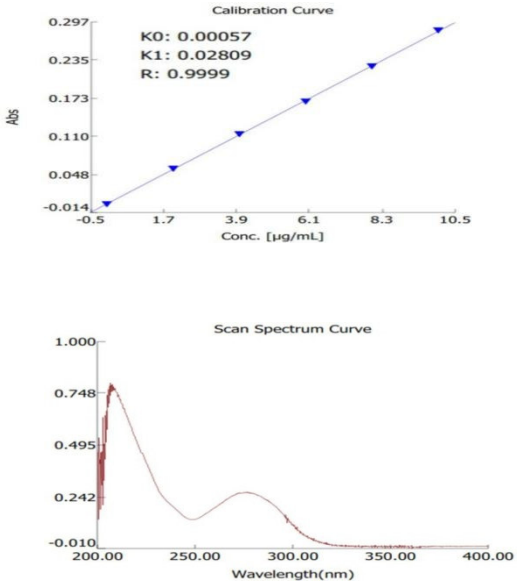
(n) were determined.

Assessment of enteric coated capsules: Enteric coated capsules were assessed at respective intervals. It's been observed from Fig.1thatcapsulesarehavingintegrity and resistance in acidic pH till 2hours.Thesafety, reliability and versatility of enteric coated capsule functional polymers can help to match your specific release profile requirements, with effective acid resistance for up to four hours. Whereas capsules in pH 6.8 were started disintegration after 1 hour. Assessment confirms that no drug release occurs during the acid stage. Rapid release then reliably occurs after conversion to pH 6.8. The high-quality capsules feature a precisely tailored enteric coating would be an ideal candidate for enteric drug delivery system.

Assessment of enteric coated capsule





Standard Graph of Diclofenac Sodium: Standard graph of Budesonide was constructed using concentration 2, 4, 6, 8, 10 (µg/ml) in6.8pHphosphatebuffer.It is evident from thefigure6&7thatthe graph is linear with regression coefficient value of R^2 = 0.9999 and slope = 0.02809 at λ max of 277nm.

Calibration Curve for Diclofenac

SUMMARY

The optimized formulation was found to b DF8 suffice the Q point criteria as per USP, according to the USP monograph of Diclofenac sodium delayed release formulation Q point criteria was given as NLT 75% at the end of 45 minutes, Formulation was designed targeting the criteria of Q point by altering the ration of hydroxyl propylmethyl cellulose and sodium starch glycolate.

CONCLUSION

The METs that were made met all of the necessary physicochemical standards, evaluation parameters helped guide the development and improvement of the MTs The optimize formulation DF8 had a drug content, solubility is in vitro and release kinetics that were acceptable. Thus we can state that the formulation is ready for testing its stability and pharmacokinetic parameters. ECDDT demonstrated to be a good replacement for commercially available formulations that don't need entire coating methods to deliver drugs that sensitive to acids

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