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Short communication

Formulation and characterization of Cefadroxil 500mg capsules prepared from final encapsulation blend

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Introduction

Cefadroxil is a semi-synthetic, β-lactam antibiotic belonging to the first-generation cephalosporins. It exhibits bactericidal activity by inhibiting bacterial cell wall synthesis (de Marco BA, Salgado HR.,2017).

The active pharmaceutical ingredient (API) is obtained via fermentation and contains 95.0-102.0% of cefadroxil on an anhydrous basis. The molecular weight is 363.4 g/mol (anhydrous), 372.4 g/mol (hemihydrate), and 381.4 g/mol (monohydrate) (Ph. Eur., 2019).

Cefadroxil monohydrate is a white or almost white crystalline powder with low aqueous solubility (0.399 mg/mL), slight solubility in ethanol (96%), and practical insolubility in chloroform and diethyl ether. It has a melting point of approximately197°C, log P of 0.4, and pKa values of 3.45 (acid) and 7.43 (base). It is commonly formulated as capsules, tablets, and powder for oral suspension.

The aim of this study was to formulate Cefadroxil 500 mg hard gelatin capsules using a dry blending process and to characterize the final encapsulation blend and finished product in order to evaluate their suitability for manufacturing and compliance with European Pharmacopoeia requirements.

Materials and methods

Pre-formulation studies of the API

Pre-formulation characterization was performed using the Certificate of Analysis for Cefadroxil monohydrate compacted as a reference. Additional testing included: Particle size distribution (PSD) analysis using MasterSizer 3000 (Malvern, UK) on three consecutive samples from the same API batch, Microscopic analysis using Zeiss Axioscope 5 microscope, and FTIR spectroscopy using Thermo Scientific iS50 with ATR diamond crystal module (range: 4000-550 cm^{-1}).

Preparation of final blend and capsules

Three consecutive batches of final blend were prepared for encapsulation into three consecutive batches of Cefadroxil 500 mg hard gelatin capsules. All ingredients were weighed and sieved through a 1.0 mm sieve (Russell Finex, UK). The mixture was blended for 10 minutes at 20 rpm using a barrel-homogenizer (Pharmatech, UK). Encapsulation from final blend was performed using a capsule filling machine (Macafor Romaco CD60, Italy) into size N^0 „0" under a vacuum of −0.2 to −0.4 bar.

The final encapsulation blend was evaluated for: Particle size distribution (d10, d50, d90) via sieve analysis (Retsch AS 200 Control, Germany), Flow properties (Ph. Eur. 10.0, Method 2.9.36.), Bulk and

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tapped density, Carr index, Hausner ratio, Loss on drying LOD (Ph. Eur. 10.0, Method 2.2.32). Carr index was calculated from bulk and tapped density (Ph. Eur. 10.0, Method 2.9.34).

Hard gelatin capsules as a final product were tested for appearance, uniformity of mass (Ph. Eur. 10.0, Method 2.9.5), disintegration (Ph. Eur. 10.0, Method 2.9.1), uniformity of dosage units and dissolution (Ph. Eur. 10.0, Method 2.9.3).

Results and discussion

Characterization of the final encapsulation blend

The final blends demonstrated good and acceptable flow properties for capsule manufacturing. LOD showed consistent values across the three consecutive batches using a halogen moisture analyzer (Mettler Toledo HS153): 2.7% (Batch M), 2.5% (Batch N), and 2.8% (Batch L), with an average of approximately 2.6%.

Evaluation of Cefadroxil 500 mg capsules

Appearance. All capsule batches showed a uniform appearance consisting of a light blue opaque body and blue opaque cap filled with light yellow powder.

Uniformity of Mass. The test was performed on 20 capsules per batch. Based on the measurements obtained during manufacturing, the minimum, maximum and mean values of the fill masses were calculated for each batch. Mean fill masses were: 592.11 mg (Batch M), 593.97 mg (Batch N), and 593.31 mg (Batch L). Variability was low, ranging from ±0.37% for Batch M, −0.57% to +0.56% for Batch N, and −0.49% to +0.42% for Batch L. All capsules complied with pharmacopoeial requirements, as no individual capsule deviated from the average mass by more than the permitted limits of 7.5% (or 15% where applicable), demonstrating excellent mass uniformity across all batches.

Disintegration. Disintegration testing was performed in water at 37± 2°C on a solid dosage form disintegration tester (Erweka ZT 322, Germany). All capsules disintegrated within 30 minutes i.e. the average time was about 8 min: 8 min 16s (Batch M), 8 min 13s (Batch N), 8 min 10s (Batch L) i.e. it complied with pharmacopoeial requirements.

Uniformity of Dosage Units. Uniformity of dosage units was evaluated using the *Mass variation* method (Ph. Eur. 10.0, Method 2.9.40). Acceptance value (AV) for all three batches is below the acceptance limit AV ≤ 15% (Batch M: AV =3.38, Batch N: AV=3.57, Batch L:AV =3.91), confirming compliance.

Dissolution. Dissolution was performed using the Basket method in a solubility test apparatus (ERWEKA, Germany) using, in medium: 900 mL water, with a rotation speed of 100 rpm, for 45 min, at a temperature of 37 ± 2°C. Average percentage of drug released after 45 minutes for each batch (Batch M: 96.15%, Batch N: 97.6%, Batch L: 101.0%), ranged from 92.2% to 102.6%, meeting pharmacopoeial requirements.

Conclusion

Three consecutive batches of Cefadroxil 500 mg capsules were successfully developed using a dry mixing process followed by encapsulation into hard gelatin capsules. The final encapsulation blends demonstrated acceptable flowability and loss on drying which indicating good moisture control and blend stability, confirming their suitability for capsule manufacturing. All capsule batches complied with Ph. Eur. requirements for: appearance, uniformity of mass, disintegration, uniformity of dosage units, dissolution. The obtained results confirm the suitability and robustness of the proposed formulation and manufacturing process.

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