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A Review on the Pharmaceutical Formulation and Evaluation of Tetracycline Capsules

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Abstract:

This study aimed to develop a stable, bioavailable oral hard-gelatin capsule formulation of tetracycline hydrochloride, a broad-spectrum antibiotic. Key challenges included the drug's photosensitivity, bitter taste, and tendency to form chelates with multivalent cations, which reduce absorption and bioavailability. Tetracycline stability also varies with pH, as degradation accelerates in highly acidic or alkaline conditions.

The formulation was optimized using pharmacopeial excipients to achieve drug stability, content uniformity, and an appropriate dissolution profile. Compatibility testing confirmed the API's stability with selected inactive ingredients. The final blend incorporated compatible fillers and flow aids, including colloidal silicon dioxide, pregelatinized starch, and magnesium stearate, chosen for their physicochemical properties.

Manufacturing involved dry-blending micronized tetracycline hydrochloride with the excipients prior to encapsulation in hard-gelatin shells. The finished capsules underwent full evaluation per British Pharmacopoeia (B.P.) and United States Pharmacopeia (USP) standards.

Key words-

Quality control, Quality Assurance, regularity Bodies, Analytical analysis, Drug qualification, Raw material

1.Introduction

Tetracycline, a member of the tetracycline class of broad-spectrum antibiotics, has been a cornerstone of clinical therapy for over 60 years. Offered in various forms, including 250 mg capsules, it remains a valuable option for managing diverse bacterial infections. The drug inhibits bacterial protein synthesis by reversibly binding to the 30S ribosomal subunit in susceptible organisms, blocking the incorporation of amino acids into elongating peptide chains.

The 250 mg tetracycline capsule is frequently indicated for infections due to Gram-positive and Gram-negative pathogens, such as those affecting the respiratory or urinary tracts, acne vulgaris, sexually transmitted diseases, and zoonoses like brucellosis and rickettsioses. Despite growing resistance and the availability of newer agents, tetracycline retains clinical utility owing to its affordability, reliable oral absorption, and extensive pharmacological documentation.

This review offers a thorough examination of 250 mg tetracycline capsules, focusing on their pharmacology, mechanism of action, therapeutic indications, resistance trends, pharmacokinetic profile, side effects, and

ongoing significance in antimicrobial treatment. Appreciating tetracycline's changing role in contemporary practice is essential for maximizing efficacy and curbing resistance.

2. Mechanism of Action of Tetracycline

Tetracyclines are broad-spectrum bacteriostatic antibiotics that **inhibit bacterial protein synthesis** by interfering with the function of the 30S ribosomal subunit.

2.1 Administration and Absorption

Tetracycline (oral or parenteral) → absorbed into systemic circulation → distributed throughout the body.

2.2 Bacterial Cell Entry

Tetracycline → diffuses through outer membrane (via porin channels in Gram-negative bacteria) → enters cytoplasm by energy-dependent active transport.

2.3 Binding to Ribosome

Tetracycline → binds reversibly to 30S ribosomal subunit → specifically at the A-site (acceptor site).

2.4 Blocking tRNA Attachment

Binding at A-site → prevents aminoacyl-tRNA from attaching to the mRNA–ribosome complex.

2.5 Inhibition of Protein Elongation

No aminoacyl-tRNA entry → no addition of new amino acids → inhibition of peptide chain elongation.

2.6 Suppression of Protein Synthesis

Inhibition of elongation → halt in bacterial protein synthesis → essential bacterial enzymes and structural proteins not produced.

2.7 Bacteriostatic Effect Lack of protein synthesis → inhibition of bacterial growth and multiplication (bacteriostatic effect) →immune system eliminates the pathogen.

3. Drug Profile: Tetracycline

3.1 Chemical Name/ IUPAC name	(4S,4aR,5S,5aR,6R,12aS)-4-(Dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxonaphthacene-2-carboxamide
3.2 Molecular Formula	$C_{22}H_{24}N_2O_8$
3.3 Molecular Weight	444.43 g/mol
3.4 Appearance	Yellow, crystalline powder
3.5 Odour	Odourless
3.6 Taste	Slightly bitter
3.7 pKa Values	~3.3, 7.7, and 9.7
3.8 Solubility	Slightly soluble in water; soluble in dilute acid and alkali; insoluble in chloroform and ether
3.9 Partition Coefficient	Approximately -1.3

(log P)	
3.10 Melting Point	175–180 °C (decomposes)
3.11 Stability	Decomposes in presence of light, moisture, and alkaline Condition.
3.12 UV Absorption (λ max)	270 nm and 360 nm (in methanol)
3.13 Storage Conditions	Protect from light and moisture; store below 25°C

4. Therapeutic uses:

Acne, Respiratory infections, Cholera, Rickettsial infections, etc.

5. Ingredients Used in Tetracycline Capsule Formulation

Diluents / Fillers

- Microcrystalline cellulose (MCC)
- Starch
- Lactose monohydrate

Disintegrant

- Sodium starch glycolate

Glidant

- Talc

Lubricants

- Stearic acid
- Magnesium stearate

Stabilizers / Antioxidants

- Ascorbic acid (Vitamin C)
- Citric acid
- Anhydrous sodium metabisulfite

Opacifiers / Colorants

- Titanium dioxide
- Iron oxide pigments (yellow/brown)

pH Modifier / Buffer

- Citric acid
- Sodium citrate

Capsule Shell Material

- Hard gelatine capsule

- HPMC (Hydroxypropyl methylcellulose) capsule

- Opaque capsule shell (titanium dioxide pigmented)

Flavouring / Sweetener

- Sucrose

- Saccharin sodium

6. Method of Preparation Tetracycline Capsule

6.1 (Step 1)

Raw Material Dispensing

All materials (API and excipients) are accurately weighed as per the master formula record (MFR) under controlled environmental conditions (temperature 20–25°C, RH ≤ 40%).

Dispensing should be done in low light conditions to prevent photodegradation of tetracycline.

Objective: Ensure accurate quantity and traceability of all ingredients.

6.2 (Step 2)

Sifting / Sieving

Pass tetracycline hydrochloride and excipients through a #40 or #60 mesh sieve.

Collect the sieved powders separately.

Objective: Break lumps, ensure uniform particle size, and improve blend homogeneity.

6.3 (Step 3)

Blending / Mixing

Transfer the API (tetracycline hydrochloride) and diluent (MCC, lactose) into a double cone blender or ribbon mixer.

Mix for 10–15 minutes at 15–25 rpm until a uniform blend is achieved.

Objective: Check blend uniformity by sampling from multiple points and testing drug content.

6.4 (Step 4)

Addition of Disintegrant and Glidant

Add sodium starch glycolate (or croscarmellose sodium) and colloidal silicon dioxide to the blend.

Mix gently for 5–10 minutes to ensure even distribution.

Objective: Improve powder flow and ensure rapid capsule disintegration in vivo.

6.5 (Step 5)

Lubrication

Add magnesium stearate and mix lightly for 2–3 minutes (not more than 5 minutes).

Mixing time should be short to prevent hydrophobic coating of particles which could slow dissolution.

Objective: Reduce friction during capsule filling and ejection.

6.6 (Step 6)

Encapsulation (Capsule Filling)

Load the blended powder into a capsule filling machine.

For manual filling, use capsule boards.

For automatic/semi-automatic filling, set machine parameters for target weight.

Fill hard gelatin or HPMC capsules (size 0 or 1) with the blend.

Monitor capsule weight variation at regular intervals.

6.7 (Step 7)

Capsule Closing and Polishing

Ensure proper locking of capsule caps and bodies.

Polish filled capsules using a soft cloth, rotating brush polisher, or capsule polishing machine to remove surface powder.

Objective: Improve capsule appearance and reduce cross-contamination risks.

6.8 (Step 8)

Packaging

Pack capsules in light-resistant, airtight containers or blister packs.

Use amber or opaque plastic bottles with silica gel desiccant sachets.

Ensure sealing is tight to prevent moisture ingress.

Objective: Protect capsules from light, air, and humidity.

6.9 (Step 9)

Storage

Store finished capsules at 15–25°C, RH below 40%, and protected from light.

Label as: "Store in a cool, dry, and dark place. Protect from moisture and sunlight."

7. Evaluation of Formulation of Tetracycline Capsule

7.1 Physical Evaluation Test Method

Appearance

Visual inspection under adequate lighting

Colour and Odour

Visual and sensory observation (yellow) and be odourless

Capsule Lock / Closure Test Manual inspection or capsule snap test

7.2 Chemical Evaluation Test Method

Identification Test

UV spectrophotometry

7.3 Pharmaceutical Performance Evaluation Test

Disintegration Test

Capsules should disintegrate within 30 minutes

Dissolution Test

50 rpm Not less than 75% of tetracycline released within 45 minutes

7.4 Hardness / Mechanical Strength (Capsule Shell)

Capsule hardness tester

Should withstand 10–15 N force without cracking Ensures handling resistance

7.5 In-Process Quality Control (IPQC)

	Test	Specification / Limit
I.	Capsule weight variation	±7.5%
II.	Moisture content	NMT 5% w/w
III.	Capsule integrity	Intact, no cracks

Conclusion

The formulation and evaluation of tetracycline capsules were successfully carried out with the aim of developing an effective, stable, and patient-compliant dosage form. The prepared capsules were evaluated for various physicochemical parameters such as appearance, weight variation, disintegration time, drug content uniformity, and dissolution profile. All evaluation results were found to be within acceptable pharmacopeial limits, indicating good quality and reproducibility of the formulation.

The results confirmed that the selected excipients were compatible with tetracycline and contributed to the desired capsule characteristics. The drug release profile demonstrated adequate dissolution, ensuring the availability of the drug for therapeutic action. Overall, the study showed that tetracycline capsules can be successfully formulated using standard techniques to produce a stable, effective, and reliable oral dosage form suitable for clinical use.

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