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Review Article of D-Pencillamine Capsules

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ABSTRACT

The D-pencillamine capsules is a medicament which is used to treat wilson's disease (too much copper in the body) and rheumatoid arthritis. Also, it is used to prevent kidney stones. It is a copper chelating agent with a gold like action in RA, but bone erosion does not heal. Penicillamine is used in the treatment of medical problems such as wilson's disease (too much copper in the body) &rheumatoid arthritis. Also, it is used to prevent kidney stones

KEY WORDS:D-PENCILLAMINE CAPSULES

INTRODUCTION TO D-PENCILLAMINE CAPSULES:

Penicillamine can be used as a disease-modifying antirheumatic drug (DMARD) to treat severe active rheumatoid arthritis in patients who have failed to respond to an adequate trial of conventional therapy, although it is rarely used today due to availability of TNF inhibitors and other agents, such as tocilizumab and tofacitinib. Penicillamine works by reducing numbers of T-lymphocytes, inhibiting macrophage function, decreasing IL-1, decreasing rheumatoid factor, and preventing collagen from cross-linking.

RHEUAMATOID ARTHRITIS

Rheumatoid arthritis is an ongoing, called chronic, condition that causes pain, swelling and irritation, called inflammation, in the joints. But it also can damage other parts of the body. These may include the skin, eyes, lungs, heart and blood vessels. Rheumatoid arthritis is an autoimmune condition, which means it's caused by the immune system attacking healthy body tissue. Rheumatoid arthritis affects joint linings, causing painful swelling. Over long periods of time, the inflammation associated with rheumatoid arthritis can cause bone erosion and joint deformity.

SYMPTOMS:

- Malaise.
- Warmth in your joints.
- Joint swelling.
- Reduced range of motion.
- Joint tingling &numbness.
- Joint tenderness and pain.
- Shooting pains in the joints.

ETIOLOGY:

The exact cause is unknown, but several factors may contribute:

Genetic factors: certain genes like HLA-DR4 increase risk.

Environmental factors: smoking, Infections, and possibly stress. Hormonal factors: more common in women, possibly influenced by estrogen.

PATHOPHYSIOLOGY:

- T &B Cells favour the production of autoantibodies &cytokines (especially IL-6, IL-17).
- Overproduction of pro inflammatory cytokines including TNF&IL-6.
- Cartilage distruction and bony erosion.
- Inflammatory pathways initiated.
- Proliferation of synovial cells in joints.
- Pannus formation (osteoclast rich portion of synovial membrane).
- Cartilage destruction and bony erosion.
- Manifestation of RA clinically in the form of chronic inflammation and associated symptoms

D-PENCILLAMINE CAPSULES:

It is a copper chelating agent with a gold like action in RA, but bone erosion does not heal. Penicillamine is used in the treatment of medical problems such as wilson's disease (too much copper in the body) &rheumatoid arthritis. Also, it is used to prevent kidney stones. Chemical Name: (2S)-2-amino-3-mercapto-3-methylbutanoic acid.

MECHANISM OF ACTION:

It inhibits macrophages, decreases IL-1 and the no of T-lymphocytes, &prevents collagen cross linkage. In RA, it can depress T-cell activity, although its precise MOA is remains unknown.

PREFORMULATION STUDIES OF D-PENCILLAMINE CAPSULES:

A preformulation study is the investigation of a drug's characteristics to help design a safe, effective, and stable dosage form.

1.ORGANOLEPTICPROPERTIES:

Colour: White or off white, crystalline powder.

Odor: Slight sulfur-like odor

Taste: It is not typically evaluated due to toxicity.

2.COMPATIBILITY STUDIES:

The compatibility between drug and excipients was determined by using FTIR spectroscopy in the ratio of 1:1.

3.CHEMICAL PROPERTIES:

Molecular formula:C5H11NO2S

Molecular weight:149.21 g/mol

pka &ionization:

pka of (COOH):2

pka of(amine):7.9

pka of (thiol):8.1

Partition coeffient (log p):

Log p: approximately-2.0 indicates it is hydrophillic and may have limited membrane permeability.

4.PHYSICAL PROPERTIES:

Solubility:

Water solubility: freely soluble

pH-dependent solubility: more soluble in alkaline pH.

Melting point:198.5ºC(decomposes), indicating thermal instability

Particle size and flow properties: evaluated using microscopy, sieve analysis

Hygroscopic: needs protection from moisture.

5.STABILITY STUDIES:

Oxidation:D-penicillamine can undergo spontaneous oxidation in air to form D-pen disulfide.

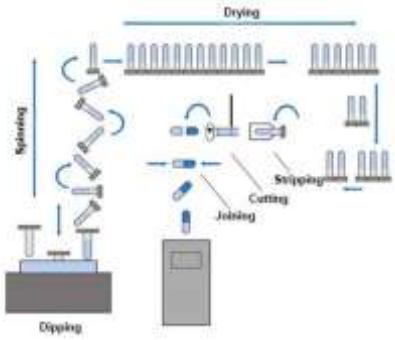
Stability of Metal Complexes: Penicillamine can form stable metal complexes, especially with copper, iron, and mercury.

Storage: It should be stored in a well-sealed container, protected from light.

METHOD OF FORMULATION OF D-PENCILLAMINE CAPSULES:

For formulating the d-pencillamine capsule have several steps:

1.Preparation of capsules shell:



2.FORMULATION OF FILLING MATERIAL:

Drug form: Powder, granules, pellets.

Excipient mixing (if required):

- *Diluents:* Adjust bulk (e.g., lactose).
- *Lubricants:* Improve flow (e.g., magnesium stearate).
- *Disintegrants:* Aid dissolution (e.g., croscarmellose).

❖ Sample compounding method for D-pencillamine250 mg capsules, preparing 30 capsules:

FORMULATION:

INGREDIENTS	OFFICIAL FORMULA	WORKING FORMULA
D-PENCILLAMINE USP	250 MG	7.5 MG
LACTOSE MONOHYDRATE	250 MG	7.5 MG

EQUIPMENT:

- Analytical balance
- Mortar and pestle
- Capsule tray (manual capsule filling machine)
- Spatula
- Weighing boats or paper

PROCEDURE:

CALCULATIONS&CAPSULE SIZING:

- Total powder per capsule=500mg
- d-pencillamine=250 mg
- lactose monohydrate(filler)=250 mg (adjust if needed for actual bulk)

WEIGHING:

- Accurately weigh 7.5g of D-pencillamine and 7.5g of lactose

MIXING

- Use geometric dilution to blend the D-pencillamine and lactose thoroughly in the mortar.

FILLING CAPSULES:

- Load the capsule tray with empty size 0 capsules.
- Fill the capsules with the powder blend
- Cap the capsules securely

FINAL CHECK:

- Weigh a few capsules to ensure uniformity
- Inspect for completeness and proper sealing.

PACKAGING AND LABELLING:

- Store capsules in a tight, light-resistant container.
- Label with:
    - Drug name and strength (D-pencillamine250 mg)
    - Directions for use
    - Storage instructions.

EVALUATION OF D- PENCILLAMINE CAPSULES:

PHYSICAL EVALUATION:

This ensures consistency in appearance and integrity of the capsules**:**

- **Appearance:** Capsules should be uniform in color and size, free from cracks, deformation, or discoloration.
- **Weight Variation:** Each capsule is weighed to ensure dosage consistency
- **Disintegration Time**: Capsules should disintegrate within 30 minutes in simulated gastric fluid

CHEMICAL EVALUATION

Ensures the correct identity and quantity of active ingredient:

- **Identification Tests**: Chemical reaction with copper ions (forms a characteristic yellow complex).
- **Assay of Active Ingredient**: Usually performed by **HPLC or UV spectroscopy** to determine the exact content of D-penicillamine (should be within 90–110% of labeled amount).

PHARMACEUTICAL EVALUATION

Evaluates drug release and stability:

- **Dissolution Test**: Ensures the capsule releases at least 80% of D-penicillamine within a specified time (typically 45 minutes).
- **Stability Testing**: Shelf life or the expiry date of packed capsules is determined under normal storage conditions.

- **Content Uniformity**: Assures even distribution of drug among capsules (especially) important for narrow therapeutic index drugs).

STABILITY STUDIES

Stability studies of pharmaceutical products may be expressed as the time during which the pharmaceutical products retain its physical, chemical, microbiological, pharmacokinetic properties and characteristics throughout the shelf life from the time of manufacture.

STORAGE, PACKAGING AND LABELLING OF D-PENCILLAMINE CAPSULES:

STORAGE GUIDELINES

- **Temperature**: Store at controlled room temperature, between 20°C to 25°C (68°F to 77°F).
- **Container**: Keep the medication in a tightly closed container to protect it from moisture and light. Use child-resistant caps when available
- **Environment**: Store in a dry, well-ventilated area, away from heat sources, direct sunlight, and incompatible materials. Avoid storing in bathrooms or areas with high humidity

LABELING REQUIREMENTS:

- **Label Includes:**
- Drug name and strength
- Batch number
- Mfg./Exp. Dates
- Storage conditions (e.g., "Store below 25°C")
- Warning: “To be sold by retail on the prescription of a registered medical practitioner only.”
- Schedule-H warning (India)

PACKAGING STANDARDS:

- **Materials**: Use containers made of glass, polyethylene, or polypropylene. Ensure containers are leak-proof, clearly labeled, and free from damage.
- **Protection**: Packaging should protect the medication from physical damage, moisture, and contamination. For bulk storage, ensure containers are stored in a cool, dry place, away from incompatible substances.

CONCLUSION

A detailed study was conducted on D-pencillamine capsules. Penicillamine is used in the treatment of medical problems such as Wilson's disease (too much copper in the body) and rheumatoid arthritis. Also, it is used to prevent kidney stones

In this study, we describe about. Pre-formulation studies like identification and characterization method of drug, excipient drug compatibility studies, and criteria for excipient selection, formulation optimization techniques and formulation of d-pencillamine capsules were also studied. The method of preparation was studied and also it includes the evaluation, stability studies, packaging and labelling of D-pencillamine capsules.

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