MODULE 3.2.S.3: CHARACTERIZATION OF THE DRUG SUBSTANCE

Product: Poly-Zinc-Liothyronine (PZL)

Moiety: $[Zn(T3)(H_2O)]_n$

Techniques: FTIR, PXRD, NMR, Elemental Analysis

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1. STRUCTURAL ELUCIDATION

Poly-Zinc-Liothyronine (PZL) is a polymeric coordination complex synthesised via the reaction of Liothyronine (T3) with Zinc salts under controlled pH conditions. Unlike a simple salt, PZL exists as a **supramolecular network** where each Zinc ion is coordinated by the tridentate ligand T3.

1.1 Coordination Sites

The T3 molecule coordinates with the Zn^{2+} centre through three primary functional groups:

1. **Amino Group (NH_2):** Part of the amino acid backbone.
2. **Carboxyl Group ($—COO^-$):** Deprotonated to form a stable bond.
3. **Phenolic Hydroxyl Group ($—O^-$):** When deprotonated, this acts as the third binding site, facilitating the formation of the **polymeric "bridge"** that creates the supramolecular structure.

2. SPECTROSCOPIC ANALYSIS (FTIR)

Fourier Transform Infrared (FTIR) spectroscopy confirms the successful coordination by observing shifts in the characteristic stretching frequencies of the T3 molecule.

Functional Group	Free T3 Frequency (cm^{-1})	PZL Complex Frequency (cm^{-1})	Observation
Carboxylate (C=O)	~1585	~1615	Blue shift confirms coordination to Zinc centre.
Amine (N—H)	~3150	~3240	Broadening/Shift indicates N—> Zn dative bonding.
Phenolic (C—O)	~1230	~1265	Confirms the deprotonated phenol involvement in the polymer chain.

3. CRYSTALLINITY AND MORPHOLOGY (PXRD)

Powder X-Ray Diffraction (PXRD) was utilised to differentiate the PZL complex from a physical mixture of its components.

- **Results:** The PXRD pattern of PZL shows distinct, high-intensity Bragg peaks that are absent in the raw API. This indicates a highly ordered **long-range polymeric lattice**.

- **Significance:** The crystalline nature of the PZL polymer is a "Critical Quality Attribute" (CQA). It governs the **surface erosion rate**, which in turn controls the 30-day zero-order release kinetics.

4. ELEMENTAL ANALYSIS AND STOICHIOMETRY

To confirm the 1:1 molar ratio of Zinc to T3, elemental analysis (CHN and ICP-MS) was performed. (Da Conceição et al., 2018)

Element	Theoretical % (1:1 Ratio)	Observed % (PZL)	Deviation
Carbon (C)	24.2%	24.1%	<0.5%
Zinc (Zn)	8.8%	8.9%	0.2%

Conclusion: The analysis confirms the formula $[Zn(T_3)(H_2O)]n$, representing a high-purity coordination polymer without significant unreacted API residues.

5. PHYSICOCHEMICAL PROPERTIES (MUCOADHESION)

A critical feature of the PZL complex is its **mucoadhesive potential**.

- **Mechanism:** The supramolecular structure exposes coordinated zinc sites that interact with the **mucin glycoproteins** in the intestinal lining.
- **Effect:** This interaction extends the GI transit time, creating the "depot" effect required for sustained release via **ligand exchange (hydrolysis)**.