

# Nickel(II)-Complex of Ceftributen Dihydrate: Synthesis, Characterization and Thermal Study

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**ABSTRACT:** Ceftributen dihydrate is a semisynthetic, orally administered, third generation cephalosporin antibiotic which is effective against most of the pathogens causing infections in the respiratory tract. Complexation of ceftributen dihydrate (Ligand, L) was performed with hydrated Ni(II) salt (Metal, M) in the ratio of 2:1 (L:M) in aqueous medium at 90 °C. The metal complex was then characterized by spectral techniques and thermal analyses. The FT-IR spectral data of metal complex suggested the monodentate bonding of metal ion to carboxylate group. Spectral evidence also supported the formation of five-membered ring *via* coordination of metal ion to  $\beta$ -lactam nitrogen and carboxylate group of parent drug. Thermal behavior of ligand and complex were studied. Thus, thermo-analytical (DSC and TGA) results also supported the formation of new metal complex, indicating the successful interaction of metal ion to ligand.

**Key words:** Ceftributen, Ni(II)- complex, Interaction, Thermal analyses.

## INTRODUCTION

Drug research is an important field of medicinal chemistry. It includes new drug synthesis with therapeutic importance<sup>1-3</sup>, isolation of bioactive compounds from different parts of medicinal plants *via* solvent extraction<sup>4,5</sup> and metal complexation of drug with improved bioactivity.<sup>6-8</sup> Drug-drug interaction<sup>9,10</sup> is also an emerging field of drug research. Moreover, in advance study, computer aided design has been implemented to discover new drug.<sup>11</sup>

Presently metal complexation of drug is an important area of research in pharmaceutical chemistry. In this study, complexation of ceftributen dihydrate has been performed using Ni(II) salt as metal source. Ceftributen dihydrate is chemically (+)-(6R,7R)-7-[(Z)-2-(2-amino-4-thiazoyl)-4-carboxycrotonamido]-8-oxo-5-thia-1-azabicyclo(4,2,0)oct-2-ene-2-carboxylic acid, dihydrate with molecular formula  $C_{15}H_{14}N_4O_6S_2 \cdot 2H_2O$  and molecular weight 446.45.<sup>12</sup>

It is a class of  $\beta$ -lactam, orally administered third generation cephalosporin antibiotic, effective against the most of the pathogens causing infections in the respiratory tract.<sup>13</sup> Ceftributen dihydrate belongs to bactericidal antibiotic that kills bacteria through binding of essential target protein of bacterial cell wall and thus inhibits replication.<sup>14</sup>

Literature survey showed that metal complexes of nitrogen containing ligands possess a variety of range of biological properties such as antibacterial, antifungal, antitumor and antiviral activities.<sup>15-17</sup> Actually the lipophilicity of parent ligand is increased through the complexation with metal ions and thus boost up the penetration capability of the ligand into the lipid membrane of bacteria. As a result, new cell wall formation is greatly hampered. Without a cell wall, a bacterial cell is defenseless to outside water and molecular pressures, which causes the cell to die quickly.<sup>18,19</sup> Thus, the antimicrobial activity of ligands can be improved through chelation.<sup>20</sup> Even some inactive ligands may acquire pharmacological properties upon chelation.<sup>21</sup> From the literature survey, it is also revealed that pharmacologically

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