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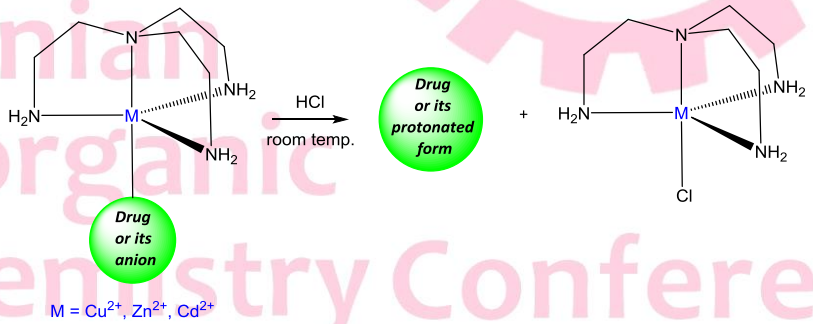
Tris(2-aminoethyl)amine-based metal complexes as new pH-sensitive drug vehicles

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Transition metal complexes can be designed as prodrugs that are inactive under normal physiological conditions but become unstable with changes in the environment such as changes in pH and redox status. By deactivating the drug before reaching the target, side reactions can be reduced, and adverse side effects can be avoided [1]. The delivery of drug favipiravir (FAV) is challenging due to its limited solubility in water and common organic solvents [2]. Given that the safety of FAV has already been demonstrated by its widespread use as an anti-influenza drug in Japan [3] further research into the more effective delivery of this drug is warranted. In an attempt to solve the delivery problem, we have used the biocompatible tris(2-aminoethyl) amine (tren) as a basic ligand for the preparation and characterization of a highly water-soluble drug-carrier complex with a zinc center that can carry the drug FAV, as an anion, and then release the molecule at a site where the pH is in the range of 3 to 5.5. We also report a theoretical study that shows the same nature of metal−ligand bonds for *N/O*-coordinated FAV and supports experimental observations indicating that FAV can easily leave the drug carrier in acidic conditions [4]. Our results indicate that this drug vehicle is suitbale for delivery of some other drugs, specially drug amifampridine.

Keywords: Tris(2-aminoethyl)amine, Favipiravir, Drug carrier, COVID-19.



Scheme 1. The release of drug or its protonated form , from a drug-carrier complex and formation of [M(tren)Cl] cation (M = Cu^{2+}, Zn^{2+}, Cd^{2+}) as a drug vehicle, in the acidic conditions.

References

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