

Synthesis, Characterization, And In Silico Studies of Tricarbonyl [η^4 -5-(N-(4-Hydroxyphenyl) Cinnamamide) Cyclohexa-1,3-Diene] Iron And Its Demetallated Form Against Leishmaniasis

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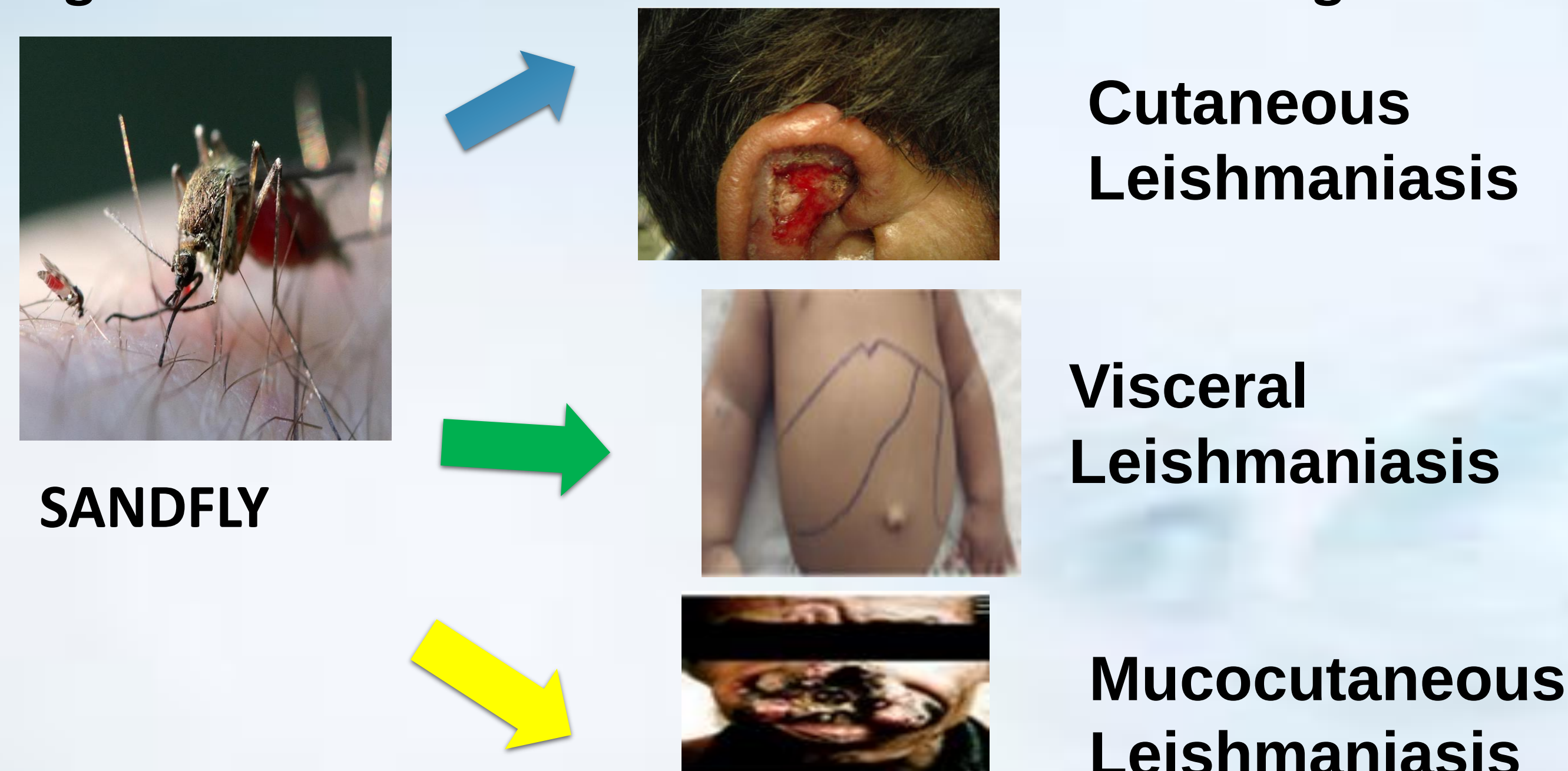
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INTRODUCTION

- Leishmaniasis is a neglected tropical disease caused by a protozoan species of the genus *Leishmania*. According to the World Health Organization (WHO), 700,000 to 1 million new cases and 26,000 to 65,000 deaths occur yearly, causing a major global public health problem. The Treatment of leishmaniasis has remained insufficient since the current antileishmanial agents have several limitations including low efficacy, toxicity, adverse side effects, drug-resistance, length of treatment and cost lines ¹.
- The most widely used Over the Counter (OTC) medication worldwide is acetaminophen which is used as an analgesic and antipyretic drug ². Chalcones is a member of the α , β -unsaturated ketone class of chemicals which is pharmacologically active ³.
- Organometallic complexes are clinically used to treat cell and tissues injuries such as leishmaniasis ⁴. Therefore, the addition of acetaminophen based chalcone to tricarbonyl (η^5 -cyclohexadienyl) Iron hexafluorophosphate may be of a great help in treating leishmaniasis.

Figure 1: Transfer of Leishmaniasis To human Being



METHODS

Figure 2: Formation of Acetaminophen based Chalcone and Adduct

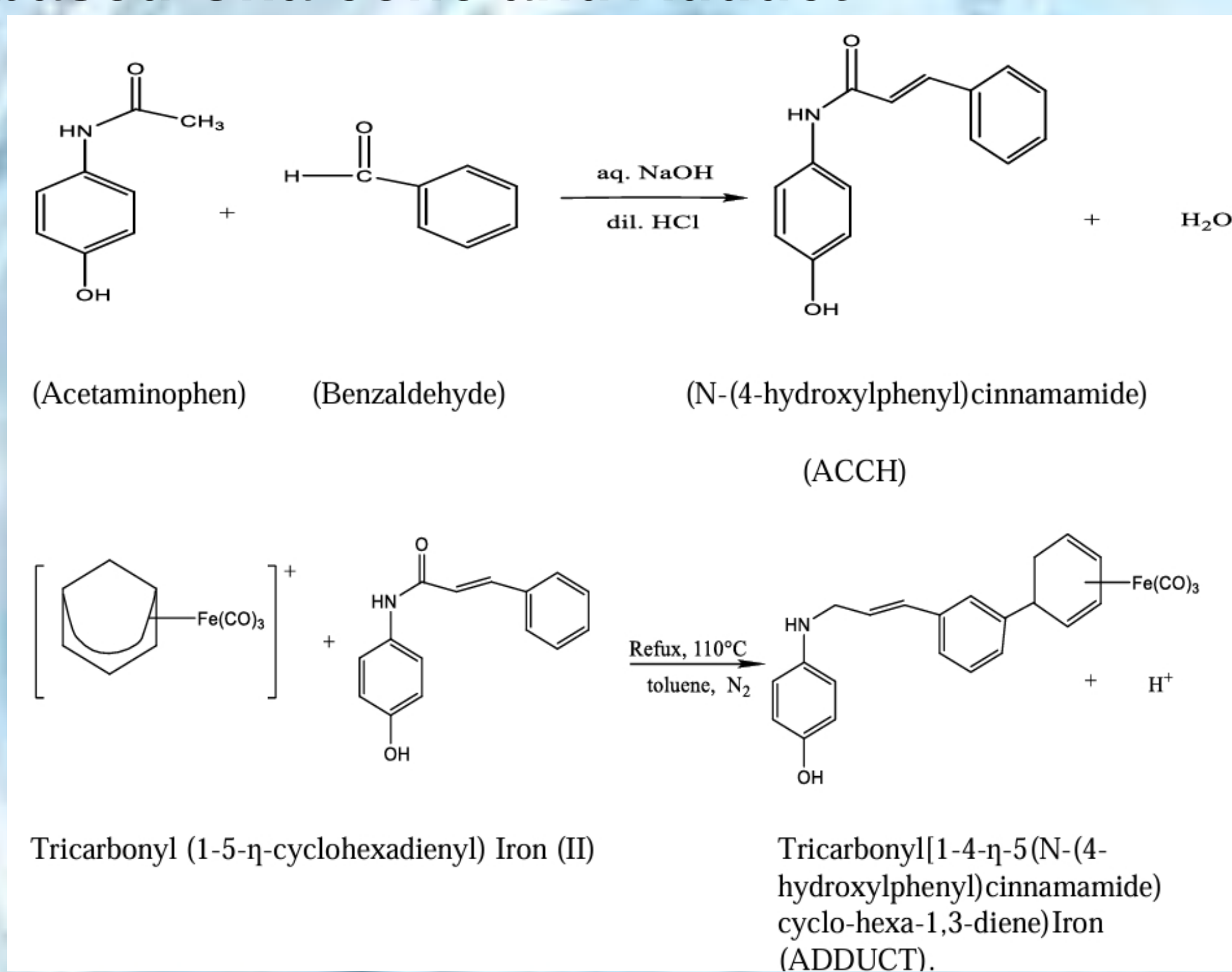


Figure 3: Demetallated Process

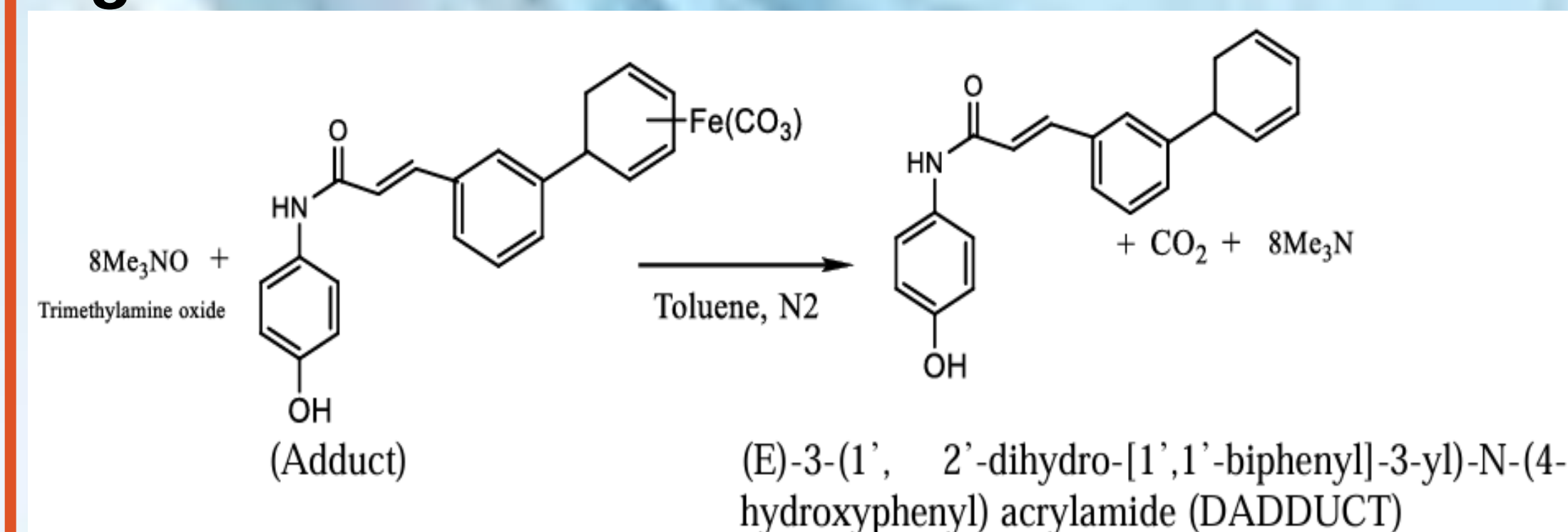


Figure 4: Computational Process



RESULTS

Table 1: Physical Data

Compounds	Molecular Formula	Percentage Yield (%)	Melting point (°C)	Molar Mass (g/mol)
ACT	C ₈ H ₉ NO ₂	-	175	151
ACCH	C ₁₅ H ₁₃ NO ₂	93.3	90	239
ADDUCT	C ₂₄ H ₁₉ FeNO	27.4	168	457
DADDUCT	C ₂₁ H ₁₇ NO ₂	32	-	315

Fig. 5

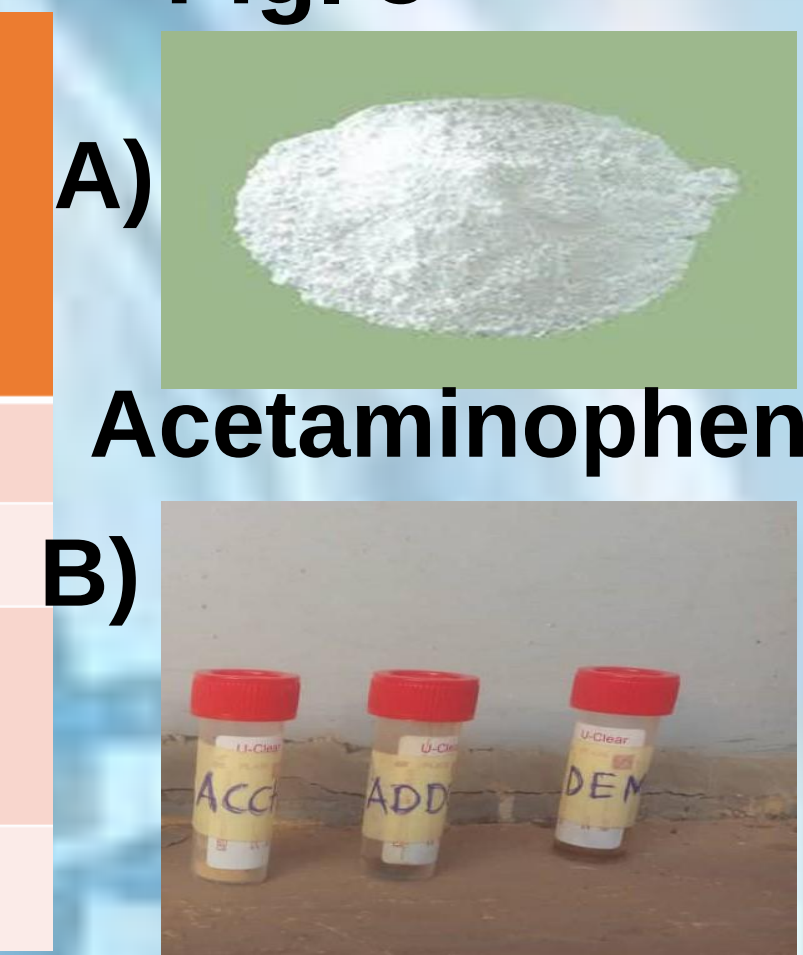


Figure 6: FTIR Analysis

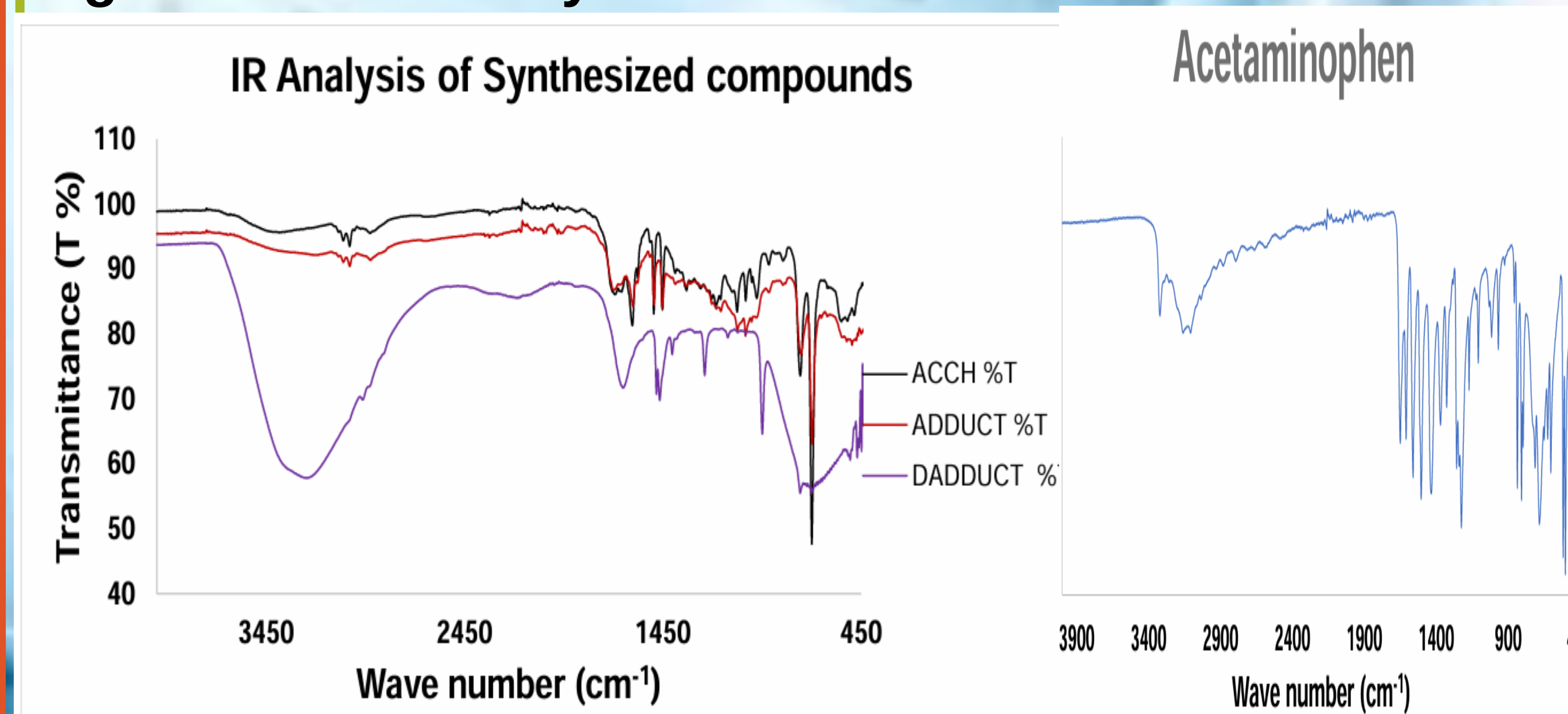


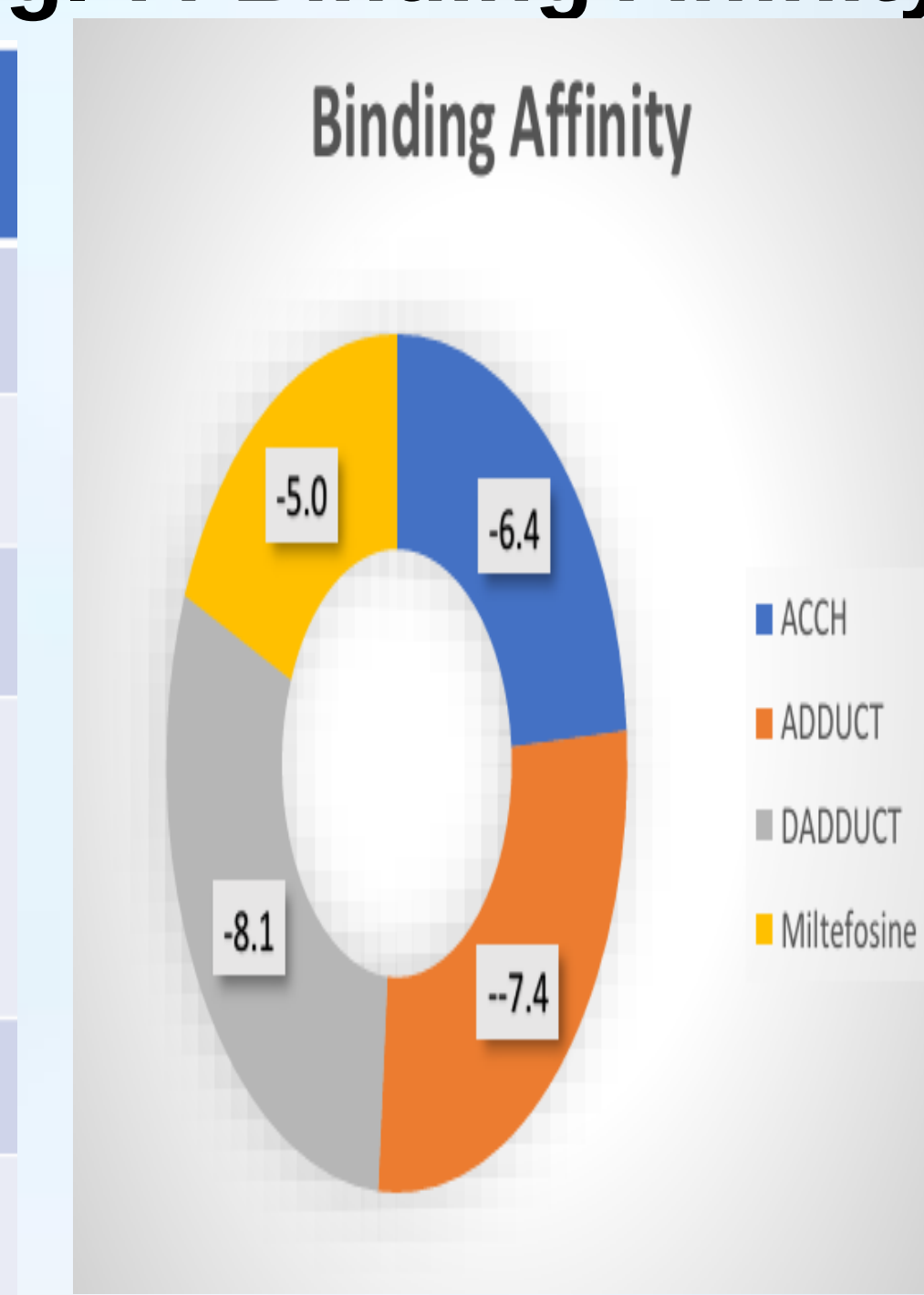
Table 2: ADME Prediction

Compounds And Standard	GIA	BBB Permanent	p-gp substrate	CYP Inhibitor	LIPINSKI Rule of five	Water Solubility
ACCH	High	Yes	No	1A2, 2C9	Yes	Soluble
ADDUCT	High	No	No	2C9	Yes	Moderately Soluble
DADDUCT	High	Yes	No	1A2, 2C9, 2C19, 3A4	Yes	Moderately Soluble
Miltefosine	Low	No	Yes	2C9, 3A4	Yes	Moderately Soluble

Table 3: Toxicity Prediction

Compounds	ACCH	ADDUCT	DADDUCT	MILTE
Mutagenicity	Yes	No	Yes	No
Cardiotoxicity	No	No	No	Yes
Immunotoxicity	No	Yes	Yes	Yes
Respiratory toxicity	No	No	No	Yes
Carcinogenicity	Yes	No	Yes	No
Neurotoxicity	Yes	No	Yes	No

Fig. 7: Binding Affinity



CONCLUSION

The disappearance of the coordinated organometallic moiety and Fe-M band show demetallation was successful. The synthesized compounds show good binding energy and interacted well within the active pocket of leishmanolysin compared to Miltefosine. The synthesized compounds show good absorption, distribution and metabolism compared to Miltefosine except the demetallated form which may cause drug-drug interaction. Adduct displays lesser toxicity compared to ACCH, the demetallated form, and Miltefosine which shows this study would be very helpful in the search for new antileishmanial drugs.

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