Drug activation for the discovery and development of new targeted chemotherapeutic formulations

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Conjugation of a drug with a metal is the key for its biological activity enhancement. Moreover, a new era was recently opened in the discovery and development of new therapeutic agents, from the combination of two distinct classes of chemical or biological agents into a single entity. This provides the opportunity for synergistic effects, most notably when one of the components acts as a detector agent of the targeted intracellular component, cell, tissue etc and the other interacting with the desired biological system. In our laboratory we are examining closely the biological activity of new such conjugates of drugs, metabolite, anti-metabolites, and natural product ingredients with metals aiming in the development of new chemotherapeutic agents.

Clinical trials and epidemiological studies have shown that Non-Steroidal Anti-inflammatory Drugs (NSAID's) exhibit protective role against the incidence of mammary cancer. The conjugation of specific NSAID's with mitochondriotropic ligands, is used for the delivery of the drugs to mitochondria as "**Trojan horse**". The low toxicity against humans of silver(I) ions enables their use in the development of new metallotherapeutics.

The synthesis of a series of silver(I) metallotherapeutics of formulae $[Ag(D)(EAr_3)_n]$, (D= salicylic acid, aspirin, diclofenac, naproxen, nimesulide etc; E= P, Sb etc; Ar= Ph-, p-tolyl-, m-tolyl, o-tolyl) is reported. The compounds were characterized by spectroscopic (NMR, IR, Raman etc) and X-Ray diffraction techniques. Theses complexes were *in vitro* evaluated for their activity against human breast cells, MCF-7 (Hormone Depended) and MDA-MB-231 (Hormone Independent). Their toxicity was evaluated against normal human cells (normal human fetal lung fibroblast cells (MRC-5)).

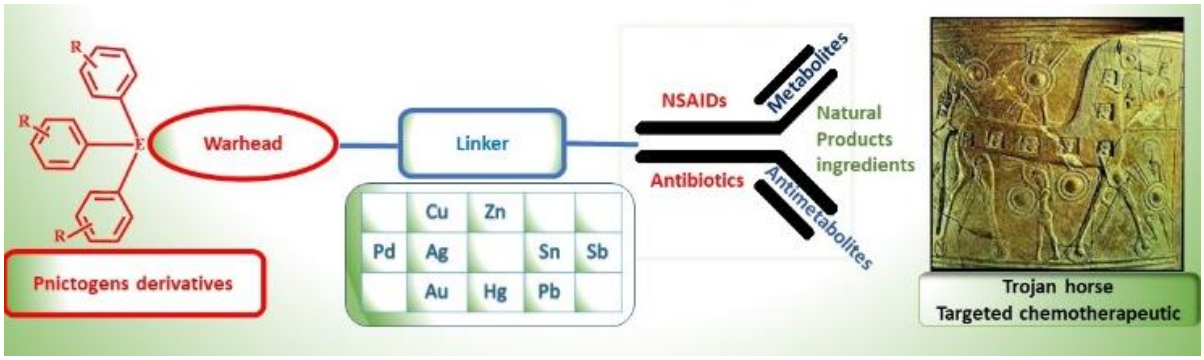

Figure. conjugation of pnictogens with NSAID in one entity

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