Medicinal importance of isonicotinoyl hydrazones.

Isonicotinoyl hydrazones play an important role in medicinal chemistry. They are used as their complexes with metal ions for the treatment of number of diseases. As these organic compounds contain nitrogen as well as oxygen, they have the ability to form complexes easily with many metal ions. The hetero atoms, nitrogen as well as oxygen can form coordinate bonds with many metal ions and thus, form stable complexes. Number of reports are available on the medicinal importance of these compounds. A brief account of these reports is presented in the following paragraphs.

Chitamber et al reported\textsuperscript{1} that pyridoxal isonicotinoylhydrazone is useful in the treatment of lymphoma and bladder cancer. According to them, transferring, an iron transport protein, increase gallium uptake by cells, whereas pyridoxal isonicotinoyl hydrazone (PIH), an iron chelator, transports iron into cells. 50 µg/ml Ga – PIH inhibited cellular proliferation by 50 percent whereas similar concentrations of PIH or gallium nitrate were not growth inhibitory. They reported that their studies suggest further evaluation of PIH as a potential antineoplastic agent.

Sterba et al\textsuperscript{2} carried out investigations relating to safety and tolerability of repeated administration of pyridoxal 2-chlorobenzoyl hydrazone (0 – 108) inhibits. The data from this study suggest that 0 – 108 remains a promising drug from the stand point of the possibility of its repeated administration and warrant further administrations.

Dimitrov\textsuperscript{3} et al carried out investigations to find out whether 3,5-dichlorosalicyldehyde isonicotine hydrazone (SH-7) an analogue of the anti tuberculosis drug
isoniazid (INH) could prevent isoniazid – induced liver damage. Forty one healthy mice were treated with solution of INH and SH – 7.

Cocco\textsuperscript{4} and coworkers studied the activities of six derivatives of a new class of isonicotinoyl hydrazones. They investigated in vitro against mycobacterium tuberculosis, isoniazid resistant mycobacterium tuberculosis ATCC 35822, rifampicin – resistant ATCC 35838, pyrazinamide resistant ATCC 35828, streptomycin resistant ATCC 35820 and sixteen clinical isolates of mycobacterium tuberculosis. They reported that this compound may serve as promising lead compound, for future development for the treatment of mycobacterium tuberculosis infections. They cited \textsuperscript{5-15} number of references to explain their activity.

Senior and Eisele\textsuperscript{16} studied the relationship between structure, disintegration and anti tuberculotic in vitro activity of over 200 derivatives of isonicotinic acid hydrazide. Conclusive evidence reflects that many compounds do not withstand the in vitro conditions.

Richardson et al\textsuperscript{17} made systematic study on pyridoxal isonicotinoyl hydrazone and its analogues. They are orally effective Fe(III) chelators which show potential as drugs to treat iron overload disease. They discussed the relationship of the partition coefficient of their iron chelators and their Fe(III) complexes.

In vitro and in vivo activity of acylated derivatives of isoniazid against mycobacterium tuberculosis was carried out by Hearn and Cynamon\textsuperscript{18}. It represents a major metabolic pathway for INH in human beings. The authors conclude that such close
structural component of metabolites of INH may serve as significant leads in antituberculor discovery and explanation of the mode of action of INH. Hearn and Cynoman\(^{19}\) prepared isoniazed Schiff base. They have evaluated its action against mycobacterium tuberculosis. They observed that acetylation greatly reduces the therapeutic activity of the drug, resulting in under doing, decreased bioavailability and acquired INH resistance. Chemical modification of INH with a functional group blocks acetylation, while maintaining strong antibacterial action. They quoted several references to prove their observations.

Blaha and Coworkers\(^{20}\) studied biliary iron excretion in rats following treatment with analogues of pyridoxal isonicotinoyl hydrazone (PIH). Over four analogs of PIH were used and some of them proved to be very potent in mobilizing Fe in vitro from Fe – 1 study. Some of them were found by the author to be very effective. Many reports are available on PIH.
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