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Review Article on Isoniazid Drug and their Different Biological Activities

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Abstract

Isoniazids are the common medication of antituberculosis used for the prevention and treatment of Mycobacterium tuberculosis infection. It is an antibiotic and work by stopping the growth of infectious bacteria. In this, the prodrug which is activated by the intracellular KatG enzyme of Mycobacterium tuberculosis. The chemical name of isoniazid is isonicotinic acid hydrazide. Isoniazid belongs to the most efficient first line antituberculosis drug with minimum inhibitory concentration. This active drug hinders the cell wall by inhibiting the Enoyl acyl carrier protein reductase (InhA). In which the drug were synthesized for antibacterial, antimicrobial, antituberculosis, anticancer & antimalarial activities. In this review, is to summarize recent isoniazid drug and their biological activities.

Keywords: Isoniazid, Mycobacterium Tuberculosis.

1. Introduction

Isoniazids are the common medication of antituberculosis used for the prevention and treatment of M. tuberculosis infection. These are rapidly absorbed and undergo N-acetylating via the cytochrome P450 system and are subject to variable metabolism rates due to genetic variation and also absorbed from the gastrointestinal tract reaching peak plasma concentration within 1-2h of ingestion. Isoniazids are the potent antimicrobial agent and one of the most commonly used a tuberculosis medication. It inhibits lipid and DNA synthesis of Mycobacterium tuberculosis resulting in inhibition of cell wall synthesis and development. It was introduced into clinical use in 1954 after which morbidity and mortality related to

tuberculosis dropped substantially and it rapidly become the mainstay of tuberculosis treatment. In 1963, isoniazid was recommended for use as monotherapy in the prevention of activation of tuberculosis in those with latent tuberculosis. Typically it is used in combination with other antituberculosis active drug to prevent the appearance of resistance. Isoniazid is an antibiotic and work by stopping the growth of bacteria. This antibiotic treats only bacterial infections. It will not work for viral infections (such as common cold, flu). It has an indirect effect on vitamin B6-dependent enzymes. Vitamin B6 is a cofactor for kynurenines, which converts tryptophan to the tryptophan-kynurenine pathway. Isoniazid, hydrazine, and the gyrometria species of mushrooms can decrease the brain concentration of gamma-amino butyric acid by inhibiting pyridoxal-5-phosphate activity, resulting in the development of severe seizure activity [1, 2].

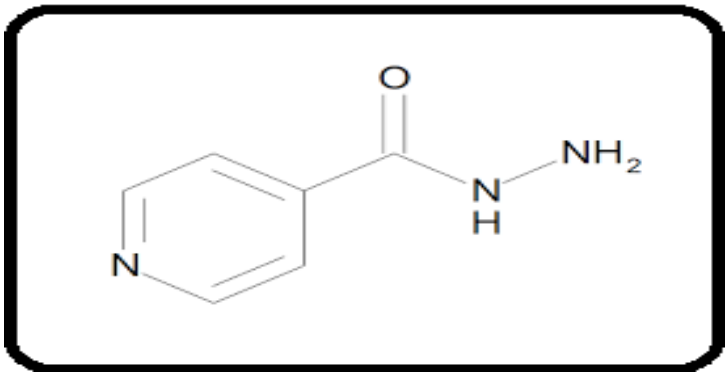

Figure.1. Isoniazid structure

Isoniazid belongs to the most efficient first line antituberculosis drug with minimum inhibitory concentration (MIC) value of 0.01-0.02 µg/ml (0.0729-1.458µm) for activity replicating Mycobacterium tuberculosis. These are most important heterocyclic moiety in organic and medicinal chemistry due to the presence of reactive site in the molecules which extends its application in various field. The interesting molecular design of isoniazid makes them acylprotein thioesterase (apt) moieties in the drug design. The chemical name of isoniazid is isonicotinic acid hydrazide. They have several other properties also which are not

much renowned such as antimicrobial, antibacterial, antivirus, antimicobacterial, antimalarial, antifungal, anticancer, antianalgesic, anticonvulsant, anticorrosive and antiinflammatory activities [3].Tuberculosis was an infectious illness distressing humanity since ancient time. According to world health organization (WHO) report, a large number of deaths worldwide are a result of the spared of tuberculosis disease caused by a single infectious bacterium. Every year, the number of cases is rising due to resistance gained by the existing anti-tuberculosis (Mtb) strains to the existing anti-tuberculosis drug. They were categorized as first, second, or third-line agents based on their discovered and efficacy in therapy. The unregulated use of anti-tuberculosis drugs in therapy for years has resulted in multidrug resistant tuberculosis. Here, we discussed the global incidences, pathophysiology of tubercular and classification, synthetic protocol, mode of action, metabolism, structure activity relationships, and toxicities of antituberculosis drugs. The traditional medications low efficacy against severely drug and multidrug resistant tuberculosis exacerbates the treatment of tuberculosis [4].One- third population amongst 7.5 billion is suffering from tuberculosis and 5000 people die with tuberculosis every day. The dispirited part of this fact is that tuberculosis is curable and advancement which have been accepted by WHO in order to prevent this disease in less span of medication. In this disease is a life threatening disease for the patients suffering from human immunodeficiency virus (HIV). In around 1.5 deaths annually caused by this bacterium due to the arrival of multidrug, drug, and extensively drug resistant in tuberculosis [5, 6, 7].

2. Biological Activities

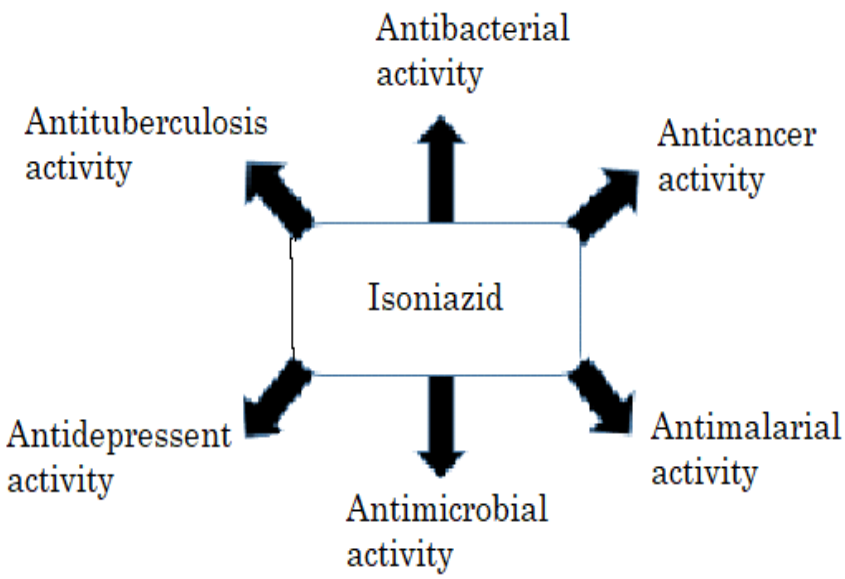

Figure.2. Biological Activities

3. Anticancer Activity

The synthetic anticancer compounds are molecularly replicated to mimic the naturally occurring compounds, with better properties, including more sustainable, cost effective, and with higher selectivity against cancer than normal cell.

4. Mechanism of Action

Mycolic acids are long fatty acids found in the cell walls of the Mycobacterium tuberculosis. The most plausible mechanism of isoniazid is the inhibition of synthesis of mycolic acid, an important constituent of mycobacterial cell wall. These produce three main types of mycolic acids: alpha, methoxy, and keto. The drug (isoniazid) acting as a prodrug which is activated by a mycobacterial catalyses peroxides to exert its lethal effect. [8, 9]

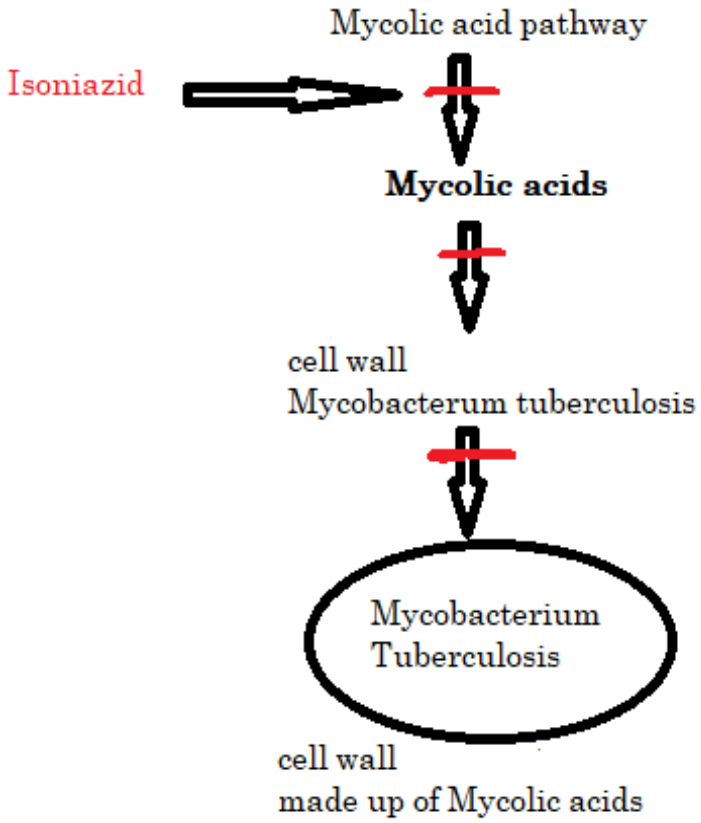

Figure.3. Mechanism of Action

5. Antidepressant Activity

Tuberculosis and depression share common risk factors, including homelessness, HIV co-infection, and alcohol and substance dependency, depression thus increases the risk for acquiring tuberculosis. Certain antidepressant can decrease the bioavailability of antituberculosis, or vice versa, due to common metabolic pathways, rifampicin for instances a powerful inducer of cytochrome P450 in the liver [10].

6. Antimalarial Activity

Antimalarial activity is aryl hydrazonechelator, 2-hydroxy-1-naphthadehyeisonicotinoyl hydrazine. It shows activity against plasmodium falciparum. It is a better antimalarial agent then well known desferrioxamines. Antimalarial activity of drugs which are well

characterized for other infectious diseases, these approaches help to reduce the time and cost required for new drug discovery. The present study evaluated the antimalarial activity antituberculosis drugs rifampicin, isoniazid, and ethambutol [11].

7. Antituberculosis Activity

Antitubercular are the antibiotic used to treat mycobacterial infections, most commonly use in combination with other antimycobaterial agents for the treatment of active or latent tuberculosis. Antibacterial agent used primarily as a tuberculostatic. In their most advantageous and commonly used as isoniazid drug, acting at the infectious site to inhibit the synthesis of mycobacterium. There are bactericidal agents active against organisms of the genus Mycobacterium, specifically M.tuberculosis, M.bovis and M.kansasii. These have highly specificity and ineffective against other microorganisms. [12]

8. Antimicrobial Activity

These studies evaluated if the enzyme mimetic activities of magnetic nanoparticles could accelerate the activation process of isoniazid against mycobacterial and, more importantly, non-mycobacterium microorganisms. First, magnetic nan-oparticles were synthesized and coated by lipoamino acid then; isoniazid was conjugated to synthesized nanoparticles [13, 14, and 15].

9. Antibacterial Activity

The Nano conjugated isoniazid was evaluated against Mycobacterium tuberculosis and four Gram-positive and Gram-negative no mycobacterial strains through a micro dilution both process. In their Results showed that the required amount of isoniazid

against Mycobacterium tuberculosis infection would decrease to 44.8% and 16.7% in conjugation with naked and surface modified magnetic nanoparticles. Also, 32 µg/mL and 38 µg/mL of isoniazid in conjugation with naked and surface-modified nanoparticles, respectively, could prevent the growth of enterococci. Hence, the vicinity of magnetic nanoparticles with isoniazid could declare promising aspects of isoniazid antibacterial capabilities [16].

10. Isoniazid Derivatives

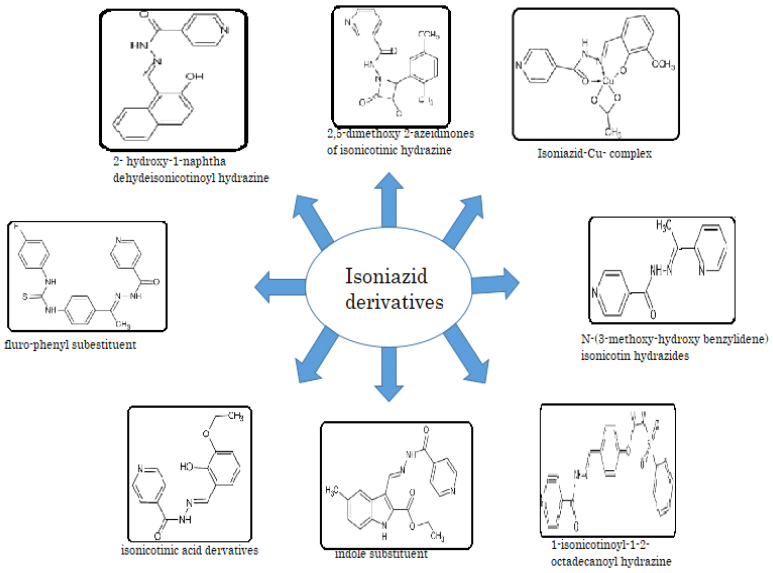

Figure.4. Isoniazid Derivatives

11. Conclusion

Tuberculosis are one of the most dangerous infectious diseases threaten throughout the world. Alarming WHO data mainly concerning an increasing number of drug-resistant, multidrug-resistant, extensively drug-resistant tuberculosis and totally drug resistant tuberculosis forms of tuberculosis, have prompted the development of novel, potent, fast acting antitubicular agents.

Isoniazid represents a unique front-line antituberculosis drug with a high specificity towards mtb. A novel set of isoniazid derivatives were synthesized and screened for antimicrobial, antimalarial, antibacterial, anticancer, antidepressant, antituberculosis and hepatic toxicity activities. We found some highly active molecules, which are evidencing to be a potent treatment of bacterial and malarial infection.

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