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A Review on Hydrazones derivative as Antioxidant Activity

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ABSTRACT: Hydrazones are an important subfamily of the Schiff-base organic molecules. The hydrazones are a very useful chemical molecule with an azomethine group (-NHN=CH-). The reactivity of hydrazone toward electrophiles and nucleophiles is a direct result of the presence of carbon in the active centers of the molecule. Heterocyclic compounds having a wide range of biological functions are only one kind of organic chemical that may be synthesized using hydrazone.
Anti-tumor, anti-inflammatory, analgesic, anti-tubercular, anti-cancer, antibacterial, and antioxidant are only some of the intriguing biological actions shown by hydrazone and its derivatives, fungicidal effects. After reacting aldehydes or ketones with hydrazide derivatives, hydrazones are produced. Every freshly produced chemical was put through pain and inflammation tests. All of the substances tested demonstrated statistically significant anti-inflammatory and analgesic effects, with derivatives demonstrating superior analgesic effectiveness to that of the standard reference chemical, acetylsalicylic acid (ASA).

I. HYDRAZONES DERIVATIVE:

When compared to conventional methods, the microwave-assisted (MW) procedure produces more fruit in less time and with fewer byproducts of chemical origin, the chemicals were only shown to have a moderate effect in inhibiting the polymerase activity of HCV NS5B. Drugs used to treat conditions such as epilepsy, depression, inflammation, malaria, mycobacteria, tumors, vascular constriction, virus infection, and schistosomiasis have all garnered significant research and development attention. An essential group of chemicals for discovering and creating novel medicines is hydrazones with an azomethine -NHN=CH- proton. Isoniazid (INH) has a very potent inhibitory action against Mycobacterium tuberculosis H37Rv when tested in living organisms. INH hydrazide was created by Sah and Peoples by the interaction of INH with a variety of aldehydes and ketones. -hydrazones. In mice infected with several M. tuberculosis strains, these chemicals were shown to limit disease progression. They were also less harmful than isoproterenol (INH) in these animals Since the -NH2 group is blocked in the produced hydrazide-hydrazones, they are less poisonous than hydrazides. Insights like this lend credence to the rising significance of the production of the f hydrazide-hydrazones complex. When it comes to biological processes, living things need iron. Deferoxamine is a medication used for "Iron Overload Disease" symptoms. Hydrazones of INH have been produced by researchers utilizing different aldehydes and their iron complexes, and their anticancer efficacy has been tested. Iron complexes block ribonucleotide reeducates, a key enzyme in the conversion of ribonucleotide to deoxyribonucleotides, which is the mechanism by which they exert their anticancer effect. We have produced and tested the antitubercular efficacy of copper complexes of INH, which enhance INH's intercellular transport. It is also possible to synthesize hydrazones by reacting aryldiazonium salts with active hydrogen molecules. A mixture of alcohol, 4-acetylphenazone, and is nicotinic acid (INH) was employed by animals) to create 4-acetylphenazone iso-nicotinoyl hydrazones by exposing the mixture to sunshine or crushing it with a mortar and pestle.

It is important to note that hydrazide-hydrazone molecules are not only useful as intermediates but also as useful chemicals. It is possible to produce coupling products utilizing the active hydrogen component of the –CONHN=CH- azomethine group when these compounds are utilized as intermediates. When hydrazones are reduced with sodium borohydride (NaBH4), N-alkyl hydrazides with various substitutes are produced. By heating hydrazones in the presence of acetic anhydride, 1, 3, 4and -oxadiazolines may be produced Azetidinones are generated through the reaction of hydrazones ethylamine choro acetyl chloride. For the synthesis of thiazolidinediones ones, hydrazones are reacted with thioglycolicolthis laccolitic acid

It is via the reduction of hydrazide-hydrazones that the synthesis of several useful chemicals, like iproniazide and isocarboxazid, is possible. Like isoniazid (INH), is thiazide is effective against TB. Patients tend to be in a better mood throughout therapy, and there is evidence that it has an antidepressant effect. Nifuroxazide, an intestinal antiseptic, is another hydrazide-hydrazone with proven therapeutic efficacy.

II. 2 ANTIOXIDANT

Because it plays such an important part in the development and upkeep of the human body, food is one of the most fundamental and essential requirements for surviving. The concept that food, in addition to supplying the body with the fundamental nutrients, may also contribute to the diverse functions of the human body is supported by a number of discoveries from study. Some fruits and vegetables are able to provide specific health advantages while also satisfying the physiological demands of the body. These foods are referred to as "Functional Food" because of their ability to do both of these things (1,2). The term "Functional Food" acts as a bridge between food and medicine due to the potential health beneficial role that is provided by the bioactive compounds and nutrients that are present in many of the plant origin foods that are available throughout the world. This role is provided by the bioactive compounds and nutrients that are present in functional foods. These effects include, but are not limited to, anti-carcinogenic, anti-inflammatory, anti-allergic, and cardiovascular protective effects, with some recent findings reporting about their anti-allergic effects as well (3–7). Anti-carcinogenic effects have also been shown to reduce the risk of developing cardiovascular disease. The protective benefits against oxidative stress derived from natural dietary antioxidants are currently receiving a significant amount of attention and concentration from researchers. Plants include natural antioxidants that have the ability to engulf and neutralize free radicals, which are unstable molecules that may cause damage to our bodies. Free radicals are species that exist independently and have one or more unpaired electrons. When free radicals interact with other molecules, they either take electrons from the other molecules or supply electrons to the other molecules. This interaction results in a wide variety of pathological conditions Researchers believe that oxidative and free radical reactions that are created are a primary factor in degenerative processes such as ageing and other illnesses such as cancer, diabetes, atherosclerosis, and others. There is a continuous production of reactive oxygen species in vivo as a result of aerobic cellular respiration, and these species can also be caused by exogenous factors such as pollution, ionizing radiation, and medicines. Living things protect themselves from this kind of damage using either their own endogenous antioxidant defence mechanisms or by consuming dietary antioxidants, which are commonly present in natural foods. It is possible to reduce one's likelihood of developing a number of chronic diseases and slow the progression of those diseases either by strengthening the body's own naturally occurring antioxidant defenses or by supplementing the diet with additional antioxidants. An important category of antioxidants is comprised of phenolic acids, flavonoids, and anthocyanins, all of which are abundant in plants and may be found in high concentrations in plant foods. Researchers are particularly interested in the phenolic compounds that are found in foods because of the powerful antioxidant effect that they have. In particular, these compounds help to combat the formation of free radicals in the human body, which in turn helps to slow down the process of cellular ageing or damage. These are a huge and diversified collection of secondary plant metabolites that are extensively distributed across the plant kingdom. Some examples of these compounds are tannins, phenolic acids, and flavonoids. The bulk of the phenolic acids that may be detected in plant tissue are made up of hydroxybenzoic acid and hydroxycinnamic acid . On the other hand, flavonoids are the most prevalent type of phenolic compound found in plants, and its structural foundation is a flavone nucleus. In terms of the hydroxylation of the nucleus and the connected sugar, the flavonoid groups are categorized as follows: isoflavones, flavanols, flavanones, catechins, anthocyanins, dihydroflavonols, chalcones, and quercetins. Tannins have the ability to tan leather as well as precipitate gelatin from solutions. The use of several of these chemicals as possible protective factors in the fight against chronic degenerative illnesses such as cataracts, diabetes mellitus, cancer, muscle degeneration, cardiovascular disorders, and neurological diseases is now being researched and investigated. A polyphenol antioxidant is another name for an antioxidant that is contained inside a polyphenolic substructure. The majority of polyphenol antioxidants may be found in foods like apples, blackberries, blues, grapes, and cherries, in addition to vegetables like cabbage, broccoli, and celery, and other similar foods. Because of Bangladesh's naturally fertile land and abundant water supply,

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the nation is home to a sizable number of different kinds of functional foods. This is because agriculture is the single most important contributor to the country's gross domestic product (GDP). Because our farmers put in a lot of effort, they are able to cultivate a broad variety of crops. As a consequence, many functional foods are cultivated here in our nation and can be purchased for very little money. It is believed that Amaranthus gangeticus, also known as lal shak in its native region, is one of the most promising sources of antioxidants among all of the fruits and vegetables that are now accessible. The inhabitants of the Indian subcontinent cultivate this green vegetable on a regular basis, and it is consumed by them either raw or cooked as a component of fresh salads or as a main course for lunch or supper. It is a member of the Flurbiprofen Hydrazones derivative family, which is a diverse group of plants that includes more than 700 different species, the majority of which have favorable benefits on one's health. It has been discovered, for instance, that plants belonging to the Alternanthera genera of the Flurbiprofen Hydrazones derivative family show significant evidence of having beneficial effects on one's health, such as antioxidant, anti-diabetic, antimicrobial, wound healing, anti-inflammatory, and a great number of other effects. Alternanthera brasiliana is a plant that is used in traditional Brazilian medicine to treat cough, inflammation, and diarrhea. Researchers have discovered that the extract of this plant has antioxidant action and that it contains a combination of beta-sitosterol, stigmasterol, and spinasterol . Alternanthera paronychioides is able to inhibit the apoptosis that is caused by glucotoxicity and is caused by reactive oxygen species in beta cells. In alloxan-induced diabetic mice, the Achyranthes aspera plant, which is a member of the Flurbiprofen Hydrazole derivative family, was found to have a hypoglycemic impact due to the powerful antioxidant activity of the isolated extract. Because it is a member of the same family as amaranths, Amaranthus gangeticus was selected to serve as the subject of this investigation. There are a great number of additional studies that support the assertion that plants in the family flurbiprofen Hydrazole derivative have powerful antioxidant qualities. Therefore, the purpose of this research is to investigate the antioxidant activity of Amaranthus Gangeticus using a variety of antioxidant assays, such as those for DPPH free radical scavenging, nitric oxide scavenging, hydrogen peroxide, and reducing power. In addition to that, high-performance liquid chromatography (HPLC), which is combined with diode-array detection, is utilized in order to identify and quantify the phenolic chemicals that are present in the ethanolic extract of this derivative.

DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity

The DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity of flurbiprofen Hydrazones derivative are given in table and figure. In the TLC-based qualitative antioxidant assay using DPPH spray, the extract of Amaranthus gangeticus showed low to moderate free radical scavenging properties as indicated by the presence of a mildly yellowish spot on a reddish-purple background on the TLC plate. Though the ethanol extract showed more significant effect compared to the ethyl acetate and toluene extract. The IC50 values of the extracts were found to be 169.3 µg/ml, ~ 47938 µg/ml and ~1.092e+017 µg/ml respectively whereas IC50 for ascorbic acid was found to be 14.76 µg/ml, which is a well-known antioxidant. The IC50 values for the ethyl acetate and toluene extracts came out to be excessively high which is not possible to obtain in a laboratory experiment and should be withdrawn as a result of some technical errors. Though Flurbiprofen Hydrazones derivative possess strong antioxidant activities, Flurbiprofen Hydrazones derivative moderate DPPH free radical scavenging effect as compared to standard antioxidants. DPPH is pink in solution and is a stable free radical, capable of accepting one electron from antioxidant containing plant extracts and thus, neutralizing its free radical nature. The degree of decolorization indicates the scavenging activity of the plant extracts and can be measured using UV spectrophotometer Hydrazones are derivative which show various kinds of biological activity such as.

Synthesis of hydrazone derivatives (N-(2,4-dimethoxybenzalidene)-2-(3-fluorophenyl-4-yl) propenamide)

0.004 mol of 2-(3-Fluorobiphenyl-4-yl) propanohydrazide was dissolved in boiling 100% ethanol. After that, 0.004 mol of 2, 4-dimethoxybenzaldehyde and 2-3 drops of glacial acetic acid were added, and the mixture was allowed to reflux for 6 hours. After being allowed to cool, the precipitate created was separated from the ethanol and recrystallized to yield the chemicals.

Synthesis of hydrazone derivatives -1

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In boiling 100% ethanol, 0.004 mol of 2-(3-fluorophenyl-4-yl) propanohydrazide was dissolved. Then 0.004 mol of 4-(N, N-dimethylamino) benzaldehyde and 2-3 drops of glacial acetic acid were added to a beaker, and the mixture was allowed to reflux for 6 hours. Compounds were obtained by filtering, drying, and recrystallizing the precipitate generated by cooling ethanol.

Compound-1	N-(2,4-dimethoxybenzalidene)-2-(3-fluorobiphenyl-4-yl)propanamide
M.F.	$C_{24}H_{23}O_3N_2F$
M.P. (ºC)	106-108
Color	Yellow
Yield (%)	75

III. PHARMACOLOGICAL ACTIVITY

Assay of free radical scavenging activity By DPPH method: -

DPPH radical scavenging activity the free radical scavenging capacity of the extracts was determined using DPPH (9). DPPH solution (0.004% w/v) was prepared in 95% ethanol. All the Hydrazones derivatives were mixed separately with ethanol, ethyl acetate and toluene to prepare the stock solution (5 mg/mL). Freshly prepared DPPH solution (0.004% w/v) was taken in test tubes and the extracts 48 were added followed by serial dilutions (1 µg to 500 µg) to every test tube so that the final volume was 3 mL and after 10 min, the absorbance was read at 515 nm using a spectrophotometer (HACH 4000 DU UV –visible spectrophotometer). Ascorbic acid was used as a reference standard and was dissolved in distilled water to make the stock solution with the same concentration (5 mg/mL). Control sample was prepared containing the same volume without any extract and reference ascorbic acid. 95% ethanol, ethyl acetate and toluene were served as blanks for each extract type respectively. The antioxidant activities were determined using DPPH, (Sigma-Aldrich, Germany; M.W.394.32M) as a free radical. Then 1µg/ml solution of Hydrazones was prepared & 6× 10-5 mol/L DPPH was prepared in methanol. 0.1 ml of Hydrazones was added to 3.9 ml of DPPH solution. Then the decrease in absorbance at 517nm was recorded at 1 min interval up to 15 minute or until the reaction is reached a level. Firstly, absorption of blank sample containing the same amount of methanol and DPPH solution was prepared and measured as a control. Ascorbic acid (Merck; M.W.176.13) was used as a standard. The experiment was carried out in triplate. Then the free radical scavenging activity was calculated by the following formula:

Percentage (%) DPPH radical scavenging activity = [(Absorbance of control -Absorbance of test Sample) / (Absorbance of control) × 100]

Result of DPPH ASSAY

Table 1 Compound [1].

Calculation of % Radical Scavening and IC50 from DPPH Assay				
Absobance Measurement Data				
Concentration (µg/ml)	Control	Sample	%RSA	IC50

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50	0.52	0.312	40	2.345
100	0.52	0.291	44.03846	7.734
150	0.52	0.228	56.15385	13.12
200	0.52	0.18	65.38462	18.51
250	0.52	0.14	73.07692	23.9
300	0.52	0.075	85.57692	29.29
350	0.52	0.035	93.26923	34.68

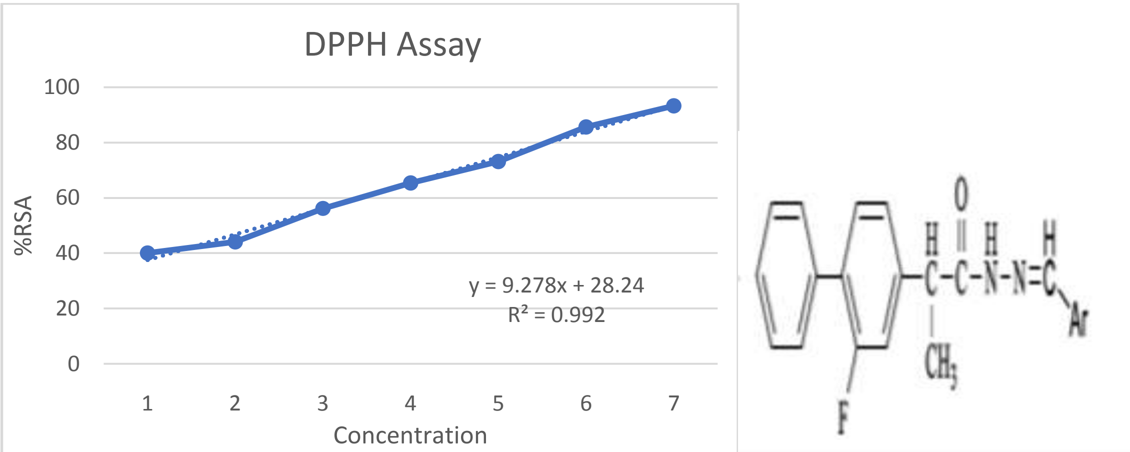

Figure (1): Showing concentration against scavengingCompound- [1]

IV. RESULT AND DISCUSSION

The compound -1 was show (NH-3197), (C-H-3020), (C=O-1658), (C=N-1620), (C-F-1078) and (C-O-1209) in characterization of FT-IR absorption bands and 1.46-1.50 (d, 3H, CH3-CH), 3.76(s, 6H,2CH3O-), 4.78-4.79 (q, 1H, CH-CH3), 6.64-8.26 (m, 11H, Ar-H), 10.23 (s, 1H, CH=N), 11.25 (s, 1H, NH)in 1H-NMR spectral data (δ ppm).

The DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity of flurbiprofen Hydrazones derivative are given in Table 3 and Figure 3. In the TLC-based qualitative antioxidant assay using DPPH spray, the extract of Hydrazone derivatives showed low to moderate free radical scavenging properties as indicated by the presence of a mildly yellowish spot on a reddish-purple background on the TLC plate. Though the ethanol extract showed more significant effect compared to the ethyl acetate and toluene hydrazones derivatives The IC50 values of the hydrazone's derivatives were found to be 169.3 µg/ml, ~ 47938 µg/ml and ~1.092e+017 µg/ml respectively whereas IC50 for ascorbic acid was found to be 14.76 µg/ml, which is a well-known antioxidant. The IC50 values for the ethyl acetate and toluene hydrazone derivatives came out to be excessively high which is not possible to obtain in a laboratory experiment and should be withdrawn as a result of some technical errors. Though Hydrazones derivative possess strong antioxidant activities, Hydrazones derivative moderate DPPH free radical scavenging effect as compared to standard antioxidants. DPPH is pink in solution and is a stable free radical, capable of accepting one electron from antioxidant containing hydrazones and thus, neutralizing its free radical nature. The degree of decolorization indicates the scavenging activity of the plant hydrazones derivatives and can be measured using UV spectrophotometer.

DPPH is a radical that has been used widely to evaluate the antioxidant activity of various Hydrazones derivatives. In this study, DPPH scavenging activity has been found in hydrazones derivatives extract due to decolorization of purple colour to yellow. In DPPH the absorbance is decreases due to presence of antioxidant activity. Due to decrease of absorbance the purple colour was turns to yellow. It was reported by (yadav et al., 2011) that DPPH absorbance is reduced by antioxidant compound or free radicals' spices to become stable diagnostic molecules resulting colour change from purple to yellow that can indicate that hydrogen denoting ability of extract sample of hydrazones. There is a significant increase in absorbance of the reaction mixture indicates the reducing power. In this experiment hydrazones have a more reducing power than the hydrazones derivatives as shown in graph.

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