Available online on 15.11.2015 at http://jddtonline.info
Journal of Drug Delivery and Therapeutics
Open access to Pharmaceutical and Medical research


REVIEW ARTICLE

# BIOLOGICALLY ACTIVE PYRIMIDINE HYDRAZONES

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Received 23 Sep 2015; Review Completed 14 Oct 2015; Accepted 15 2015, Available online 15 Nov 2015

**ABSTRACT**

**Pyrimidine** constitutes an important class of heterocycles in drug discovery & is very well known for their anticancer, antimicrobial, antioxidant & antiviral activities. **Hydrazones** is a class of organic compounds with the structure $R_1R_2C=NNH_2$. They are formed usually by the action of hydrazine on ketones or aldehydes & have efficient CNS depressant, analgesics activity. In the same context, **Schiff bases** of pyrimidine hydrazones can be prepared by the reaction of **"4-(4-Chloro-phenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxylic acid hydrazide"** with various terpenes such as **citral, camphor, furfuraldehyde** & **menthone to make Schiff bases** individually by refluxing them in the presence of glacial acetic acid (as solvent) for at least 2hrs to yield their respective derivatives.

The present studies revealed that Pyrimidine hydrazone derivatives could be used to synthesize the compounds having potent biological activities such as anticancer, antimicrobial, antioxidant, CNS depressant, analgesic & antiviral activities. All the prepared derivatives were under investigation for their antimicrobial activity and likely to possess the same & desired action.

**Keyword:** Pyrimidine Hydrazones, Biological active Pyrimidine, Schiff Bases etc.

## 1. INTRODUCTION

Medicinal chemistry is the branch of science that deals mainly with the synthetic organic chemistry and pharmacology of the drugs with special references to structure including design, modifications and analysis of drugs or chemical synthesis of lead compounds to make them suitable for the mankind or animals with least toxicity and optimum response[1].

Heterocyclic chemistry is a very important branch of organic chemistry and most of the organic synthetic or semi synthetic compounds are heterocyclic in structural properties. Its structure can be described with carbon atoms in ring forming carbocyclic compound[2].

The most common heteroatoms are Nitrogen, oxygen and sulfur. But heterocyclic rings containing other hetero atoms are having in broad variety. Heterocyclic compounds can be classified as aliphatic and aromatic. The aliphatic heterocyclics are the cyclic similarities of amines, ethers, thio ethers, amides, etc.

Heterocyclic compounds are having importance in various medicinal formulations and are present in a large variety of drugs, most vitamins, natural products etc. In addition to this biologically active compounds, including antitumor, antibiotic, anti-inflammatory, antidepressant, antimalarial, anti-HIV, antimicrobial, antibacterial, antifungal, antiviral, antidiabetic, herbicidal, fungicidal, anticonvulsant, and insecticidal agents[3].

### 1.1 Pyrimidine

Heterocyclic aromatic organic compound like benzene or pyridine, having two nitrogen atoms at positions 1 and 3 of the six-membered ring; they have isomers in the forms of diazine[4]

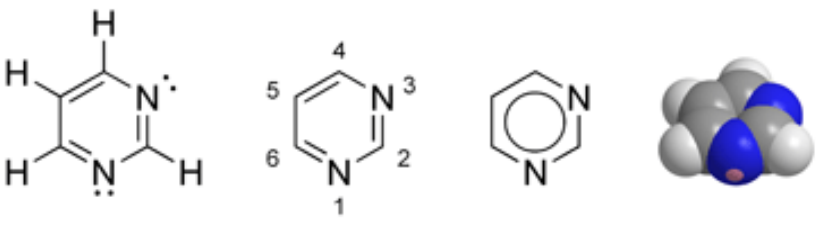


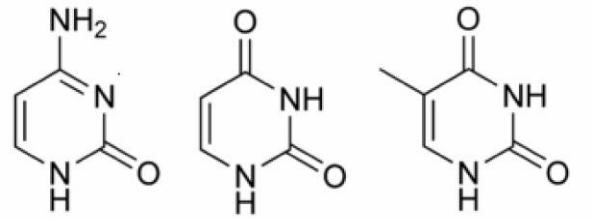

**Figure 1**

| | |
|---|---|
| IUPAC Name: | 1, 3-Diazine, m-Diazine |
| Formula: | $C_4H_4N_2$ |
| Molecular Mass: | 80.088 g mol-1 |
| Density: | 1.016 g cm-3 |
| Solublity: | Alcohol, Water |
| Melting Point: | 20-22 °C |

### 1.2 Types of Pyrimidine

Three nucleobases found in nucleic acids, cytosine (C), thymine (T), and uracil (U), are pyrimidine derivatives: [4]



**C** **T** **U**

**Figure 2**

### 1.3 Hydrazones

An organic compounds having structure of $R_1R_2C=NNH_2$ and are associated to ketones and aldehydes by substitution of the oxygen by means of $NNH_2$ functional group. They are designed basically by the feat of hydrazine on ketones or aldehydes[5].

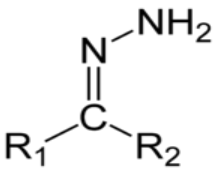


**Figure 3**

Hydrazones have antioxidant, antimicrobial, antimalarial, antiviral actions and if they are allowed to fuse with Pyrimidine they produce CNS activity too. Therefore the above data clearly showed that pyrimidine hydrazones are potent biologically active compounds.

### 1.4 Schiff base

A **Schiff base**, invented by Hugo Schiff, is a compound with a functional group that consists of a C=N double bond by means of nitrogen atom connected to an aryl or alkyl group and having general formula of $R^1R^2C=NR^3$, where R is an organic side chain. In this definition, Schiff base is identical to **azomethine**[6].

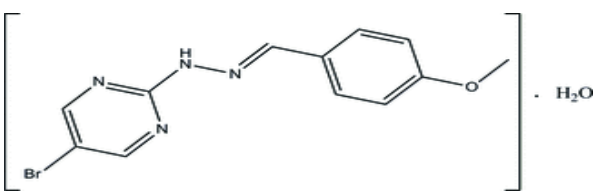
General structure of a Schiff base General structure of an azomethine

**Figure 4**

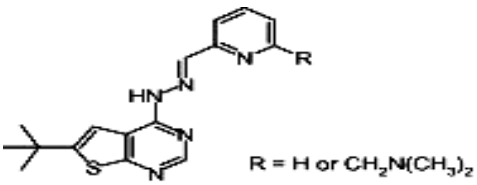
### 1.5 Some Compounds Having Pyrimidine Hydrazones

a). 4-methoxybenzaldehyde (5-bromopyrimidin-2-yl) hydrazone monohydrate[7]. Pyrimidine and their derivatives possess biological and pharmacological activities such as antibacterial, antimicrobial, anti-inflammatory, analgesic, anticonvulsant and anti-aggressive properties

$C_{12}H_{11}BrN_4O \cdot H_2O$



b). Novel thieno [2, 3-d] pyrimidin-4-yl Hydrazone-based Cyclin D1-CDK4 inhibitors [8]

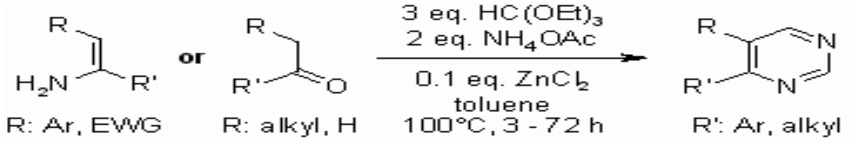


### 2. CHEMICAL APPROACHES

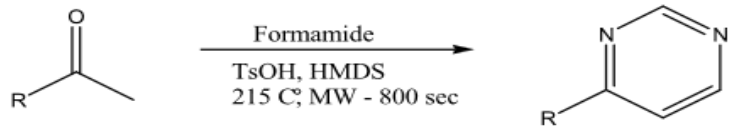
### 2.1 Pyrimidine

**2.1.1 Scheme-1:** ZnCl2-catalyzed three-component coupling reaction allows the synthesis of various 4, 5-disubstituted pyrimidine derivatives in a single step from functionalized enamines, triethylorthoformate, and ammonium acetate. The procedure can be successfully applied to the efficient synthesis of mono- and disubstituted pyrimidine derivatives, using methyl ketone derivatives instead of enamines[9]

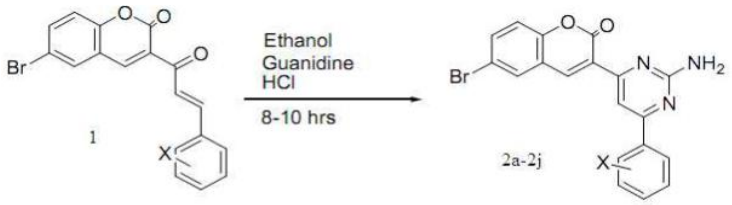
 




**2.1.3 Scheme-2:** Synthesis of pyrimidines from ketones using microwave irradiation[10]



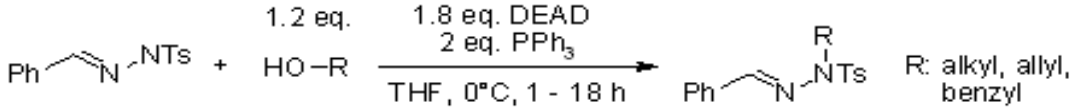

**2.1.3 Scheme 3**: Synthesis, analgesic and ulcerogenic activity of novel pyrimidine derivative of coumarin moiety: A novel series of 3-(2-amino-6-pyrimidin-4-yl)-6-bromo-2H-chromen-2-one (2a-2j) was synthesized from 3-acetyl-6-bromo-2H-chromen-2-one[11]



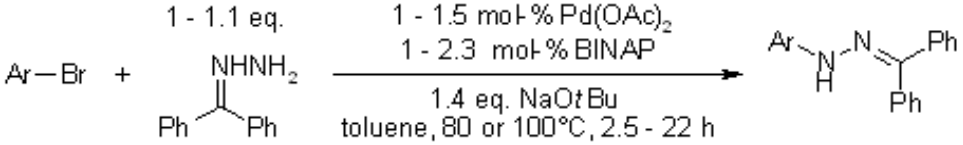

X=2-Cl, 3-Cl, 4-Cl, 2-Br, 3-Br, 4-Br, 2-$OCH_3$, 3-$OCH_3$, 2,4-Dichloro, 2,6-Dichloro

**2.2 Hydrazone**

**2.2.1 Scheme 4:** Tosyl- and Boc-hydrazones were found to be effective nucleophiles in the Mitsunobu reaction. Tosyl hydrazones reacted cleanly with primary and secondary alcohols when co-administered to a cooled DBAD/PPh3 or DEAD/PPh3 complex[12]




**2.2.2 Scheme-5:** Central to an alternative source of substrates for Fischer indolizations was a palladium-catalyzed coupling to prepare N-aryl benzophenone hydrazones. Hydrolysis of the hydrazones in the presence of ketones produced enolizable hydrazones that underwent Fischer indolization[12]

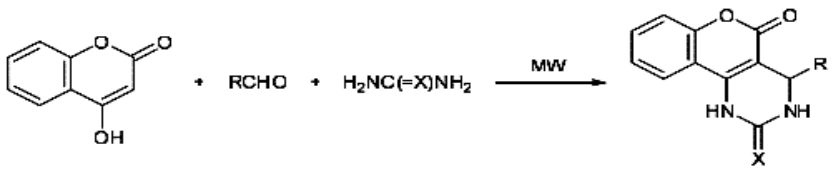



## 3. BIOLOGICAL ACTIVITY APPROACHES

### 3.1 Pyrimidine

#### 3.1.1 Biologically Active Pyridopyrimidines:

The compounds below have efficient analgesics, CNS depressant activity, and in spite of that it also exhibit antibacterial & antifungal activity[13]



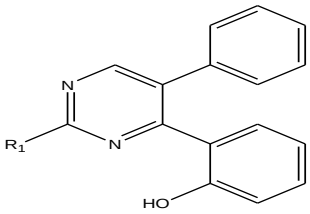

I IIa–IId IIIa–IIIh

**II**, R = Ph (**a**), 1,3-2*H*-benzodioxol-5-yl (**b**), 3-indolyl (**c**), 2-chloroquinolin-3-yl (**d**); **III**, R = Ph (**a**, **b**), 1,3-2*H*-benzodioxol-5-yl (**c**, **d**), 3-indolyl (**e**, **f**), 2-chloroquinolin-3-yl (**g**, **h**); X = O (**a**, **c**, **e**, **g**), S (**b**, **d**, **f**, **h**).

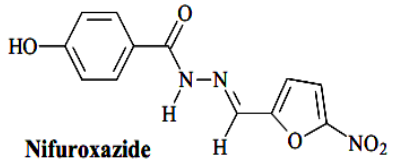
### 3.1.2 Anti-cancer activity

A series of novel 2, 4, 5-substituted pyrimidine derivatives were synthesized and evaluated for inhibition against the human hepatocellular carcinoma BEL-7402 cancer cell line[14]



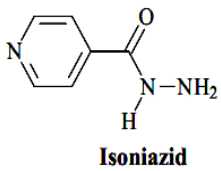

### 3.2 Hydrazone

There has been considerable interest in the development of novel compounds with anticonvulsant, antidepressant, analgesic, anti-inflammatory, antiplatelet, antimalarial, antimicrobial, antimycobacterial, antitumor, vasodilator, antiviral & antischistosomiasis activities[15]




**Nifuroxazide**

Antibiotic, Antidiarrheal

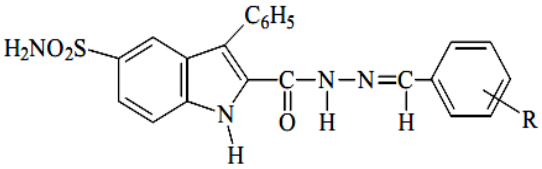



**Isoniazid**

Anti-tubercular

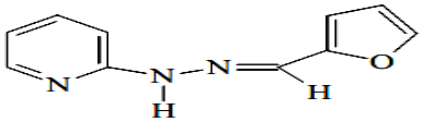
### 3.2.1 Anti-Depressant Activity

New arylidenehydrazides which were synthesized by reacting 3-phenyl-5sulfonamidoindole-2-carboxylic acid hydrazide with various aldehydes, evaluated for their antidepressant activity[15]




### 3.2.2 Analgesic, anti-inflammatory & antiplatelet activity

Derivative 2-(2-formylfuryl) pyridylhydrazone presented a 79 % inhibition of pleurisy at a dose of 80.1 µmol/kg. The authors also described the results concerning the mechanism of the action of these series of N-heterocyclic derivatives in platelet aggregation that suggests a Ca2+ scavenger mechanism[16]




## 4. CONCLUSION

**Pyrimidine** constitutes an important heterocyclic class in drug discovery & is very well known for their anticancer, antimicrobial, antioxidant & antiviral activities. **Hydrazones** is a class of organic compounds and have efficient CNS depressant, analgesics activity. In the same context, **Schiff bases** of pyrimidine hydrazones are a potent and efficient biological activities such as anticancer, antimicrobial, antioxidant, CNS depressant, analgesic & antiviral activities. There are various synthetic pathways in which various studies are made also to form a potent and efficient Schiff bases and product of pyrimidine hydrazones.

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