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DESIGN, SYNTHESIS, CHARACTERIZATION AND PHARMACOLOGICAL ACTIVITIES OF NOVEL HYDRAZONE DERIVATIVES

Navitha Alupula*[1], Ramgopal Appani[2], V. Alagarsamy[3] and B. Babu Rao[4]

[1]Department of Pharmaceutical Chemistry, Nethaji Institute of Pharmaceutical Sciences, Warangal.

[2,3]Department of Pharmaceutical Chemistry, MNR College of Pharmacy, Sangareddy.

[4]Department of Pharmacognosy, Nethaji Institute of Pharmaceutical Sciences, Warangal.

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***Corresponding Author**
Navitha Alupula
Department of Pharmaceutical Chemistry, Nethaji Institute of Pharmaceutical Sciences, Warangal.

ABSTRACT

A new series of Hydrazone derivatives**(IIIa-IIIm)** were obtained by synthesizing 2-(benzamido) benzohydrazide with different aromatic and heterocyclic aldehydes. These derivatives are characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectra. The synthesized derivatives were screened for their *in vitro* antibacterial activity against *Klebsella Pneumoniae, Salmonella Paratyphi, Escherischia Coli, Basillus Substilis* where **IIIc, IIIe** compounds showed significant activity against *Klebsella Pneumoniae.* **IIIa-IIIj** compounds were screened for their *in vitro*antifungal activity against fungal spores like *Aspergillus Nigrum, Aspergillus Clavatus, Penicillium Notatum* and *Colleotrichem Coffeanum* where **IIIa, IIIe** compounds showed significant activity against *Aspergillus Nigrum*. **IIIa, IIIl, IIIm** compounds were screened for analgesic activity among these **IIIm** compound showed significant activity. *In vitro*cytotoxic activity of **IIIb** compoundshowed significant cytotoxic activity against all the five cell lines tested in the region of 9, 23, 33, 26, 17µm for CEM, L1210, Molt 4/C8, HL60 & BEL 7402 respectively.

KEYWORDS: *Klebsella Pneumoniae, Salmonella Paratyphi, Escherischia Coli.*

INTRODUCTION

Medicinal chemistry and pharmaceutical chemistry are disciplines at the intersection of chemistry, especially synthetic organic chemistry, and pharmacology and various other biological specialties, where they are involved with design, chemical synthesis and

development for market of pharmaceutical agents. Medicinal chemistry is the application of chemical research techniques to the synthesis of pharmaceuticals.

During the early stages of medicinal chemistry development, scientists were primarily concerned with the isolation of medicinal agents found in plants. Today, scientists in this field are equally concerned with the creation of new synthetic drug compounds, possibly based on newly discovered mechanisms. The focus on development of new synthetic drug compounds has resulted in the incorporation of many other disciplines, such as biochemistry and molecular biology, into medicinal chemistry. Medicinal chemistry is almost always geared toward drug discovery and development.[1]

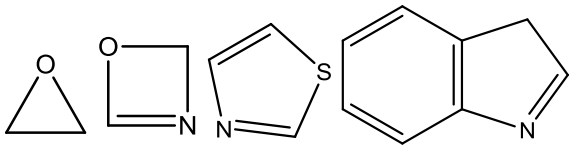
Drug discovery is the identification of novel active chemical compounds, often called "hits", which are typically found by assay of compounds for a desired biological activity. Initial hits can come from repurposing existing agents towards a new pathologic process and from observations of biologic effects of new or existing natural products from bacteria, fungi, plants, etc. In addition, hits also routinely originate from structural observations of small molecule "fragments" bound to therapeutic targets (enzymes, receptors, etc.), where the fragments serve as starting points to develop more chemically complex forms by synthesis.

Finally, hits also regularly originate from *en-masse* testing of chemical compounds against biological targets, where the compounds may be from novel synthetic chemical libraries known to have particular properties (kinase inhibitory activity, diversity or drug-likeness, etc.), or from historic chemical compound collections or libraries created through combinatorial chemistry. While a number of approaches toward the identification and development of hits exist, the most successful techniques are based on chemical and biological intuition developed in team environments through years of rigorous practice aimed sloely at discovering new therapeutic agents.[2]

Organic chemistry is a branch of chemistry that deals with the structure, properties, and reactions of compounds that contain carbon. It is a highly reactive science. Chemists in general and organic chemists in particular can create new molecules never before proposed, which if carefully, may have important properties for the betterment of the human experience.[6]

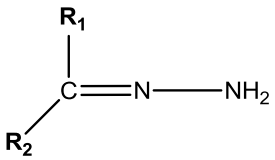
Heterocyclic chemistry

A cyclic organic compound containing all carbon atoms in ring formation is referred to as a carbocyclic compound. If at least one atom other than carbon forms a part of the ring system then it is designated as heterocyclic compound. Nitrogen, oxygen, sulphur are the most common heteroatoms but heterocyclic rings containing other heteroatoms are also widely known. Some examples of heterocyclic compounds are oxirane, 1,3 oxazete, thiazole, indole as shown in the diagrams **(1),(2),(3),(4)** respectively.[7]



(1) **(2)** **(3)** **(4)**

Hydrazones are a class of organic compounds with the structure $R_1R_2C{=}NNH_2$. They are related to ketones and aldehydes by the replacement of the oxygen with the NNH_2 functional group. They are formed usually by the action of hydrazine**(5)** on ketones or aldehydes.[3]



(5)

Hydrazones are important compounds for drug design, as possible ligands for metal complexes, organocatalysis and also for the syntheses of heterocyclic compounds. Hydrazones and their derivatives constitute a versatile class of compounds in organic chemistry.

Hydrazones contain two connected nitrogen atoms of different nature and a C-N double bond that is conjugated with a lone electron pair of the terminal nitrogen atom. Synthesis of the hydrazone derivatives is an effective way for the development of new drugs and it would be a valuable addition to the existing literature.

Hydrazones contain two connected nitrogen atoms of different nature and a C-N double bond that is conjugated with a lone electron pair of the terminal nitrogen. Hydrazones are compounds derived from the condensation of hydrazine's with carbonyl compounds namely aldehydes and ketones.

The synthesis, structure and biological activity of some new hydrazones prepared from fatty acidhydrazides has been the focus of research. Different methods have been employed to synthesize different types of hydrazones from different starting materials.

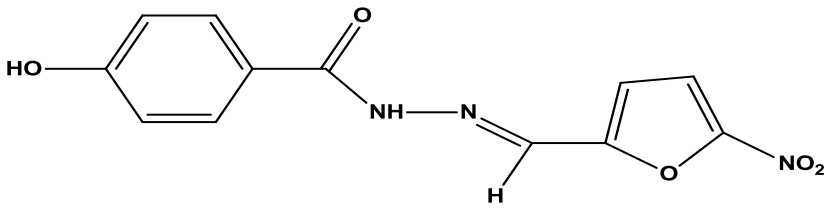
The use of fatty acid substrates as starting materials has become significant because of their own biological activity. Thus carbonyl group of methyl acetoacetate and acetyl acetone was employed to synthesize the hydrazones from the before mentioned hydrazide.

These hydrazones were also screened for their antimicrobial activity and some of the synthesized compounds showed good antimicrobial activity against *E. coli, S. aureus* and *S. albus.*

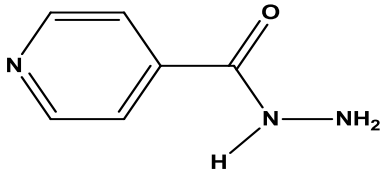
Schiff bases have a wide variety of applications in many fields, *e.g.*, biological, inorganic and analytical chemistry. Schiff bases have also been widely reported to be biologically versatile compounds possessing antifungal, herbicidal and plant growth regulating properties.

Hydrazones are a class of Schiff bases which have been found to possess many biological activities, e.g. antibacterial, anticonvulsant, anti-inflamatory, anti-platelet, anti-depressant, anti- malarial and anti-tubercular, vasodilator effect.

Thus carbonyl group of araldehydes was employed to synthesize the hydrazones from the before mentioned hydrazide. These hydrazones were also screened for their antibacterial activity, antifungal activity and some of the synthesized compounds showed good antimicrobial activity. Another clinically effective hydrazide-hydrazones is Nifuroxazide **(6)**, Isoniazid **(7)** which is used as a intestinal antiseptic.

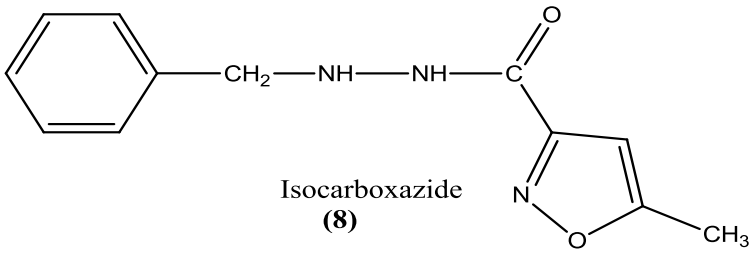


Nifuroxamide
(6)

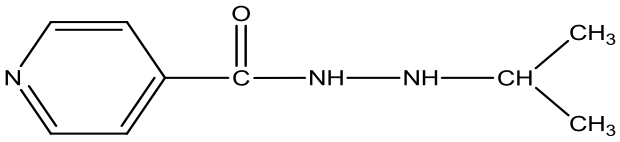


Isoniazid
(7)

Many effective compounds such as isocarboxazide **(8),** iproniazide **(9)**, are synthesized by reduction of hydrazide-hydrazones. Iproniazide, is used in the treatment of tuberculosis. It has also displays an antidepressant effect and patients appear to have a better mood during the treatment.



Isocarboxazide
(8)



Iproniazide
(9)

These structural fragments are mainly responsible for the physical and chemical properties of hydrazones. Both nitrogen atoms of the hydrazone group are nucleophilic, although the amino type nitrogen is more reactive. The carbon atom of hydrazone group has both electrophilic and nucleophilic character.

Hydrazones have attracted considerable attention in medicinal chemistry due to their distinctive structural features and a wide range of pharmacological activities. This is exemplified by the synthesis and pharmacological evaluation of a large number of hydrazine derivatives against various pharmacological targets. While a number of hydrazones have been reported to possess promising antitumor activities, the synthesis and cyto toxicities of hydrazone derivatives derived from anti-inflammatory agents have remained unexplored until recently.

For example hydrazones derived from diclofenac acid have shown anti mycobacterial activities when tested *in vitro* and *in vivo*. Recently, synthesis of a series of acyl hydrazones based on mefenamic acid, some of which showed cytotoxic properties *in vitro* especially at higher doses.

Incontinuation to identify more potent cytotoxic agents, decided toexplore the structural features of other anti-inflammatory agents that can be incorporated in target molecules. Accordingly, selected two potent anti-inflammatory agents such asNaproxen and ibuprofen, representatives of a group of NSAIDs (non steroidal anti-inflammatory drugs) that are commonly used to treat pain andother inflammatory diseases. we anticipated that combination of structural features of these NSAIDs with substituted hydrazones in a single molecule would provide novel agents possessing potent cytotoxic activities.

Here in, the synthesis, structure analysis and *in vitro* pharmacological evaluation of a series of hybrid molecules based on hydrazone. Hydrazines and their derivatives constitute an important class of compounds that has found wideutility in organic synthesis. While hydrazines have traditionally been employed as reagents forthe derivatization and characterization of carbonyl compounds, in recent years the N-N linkage has been used as a key structural motif in various bioactive agents.

In particular, an increasing number of N-N bond-containing heterocycles and peptidomimetics have made their way into commercial applications as pharmaceutical and agricultural agents. Recently, hydrazide-hydrazones have gained great importance due to their diverse biological properties including antibacterial, antifungal, anticonvulsant, anti-inflammatory, anti-malarial and anti-tuberculosis activities.

With the aim of obtaining novel hydrazide-hydrazones with a wide spectrum of pharmaceutical applications, here in the synthesis of a series of hydrazide-hydrazones together with their use in a series of heterocyclic transformations and their evaluation as anti-tumor agents.

Hydrazones exhibit physiological activities in the treatment of several diseases such as tuberculosis. This activity is attributed to the formation of stable chelate complexes with transition metals which catalyze physiological processes. They also act as herbicides, insecticides, nematocides, rodenticides, plant growth regulators, sterilants for houseflies, among other applications.

In analytical chemistry hydrazones find applications as multidentate ligands for transition metals in colorimetric or fluorimetric determinations.

The battle against the infectious diseases has become a never ending process, as microorganisms are becoming resistant more quickly than new drugs are being made available. when we look into the history and development of antibacterial agents the scientific development of antimicrobial drugs can be mainly divided into three main phases.

The first phase began with Ehrlich in 1890's the use of methylene blue for managing malaria, the organic arsenials for Trypanosomiasis (1904), and salvarsan for syphilis (1909), Atebrin was made in 1932 and used for prophylaxis of malaria.[4]

Second phase evolved with the pioneering discoveries of penicillin by Fleming in 1928. Since the discovery of penicillin of fleming, antimicrobials have been widely applied for clinical use. The number of those who die from microbial infections, which was the greatest threat to human beings, have significantly decreased and average life expectancy, has been largely extended. Before penicillin became a viable medical treatment in the early 1940's, no true cure for gonorrhea, strepthroat, or pneumonia existed. Patients with infected wounds often had to have a wounded limb removed, or face death from infections. Now, most of these infections can be cured easily with a short course of antimicrobials.

The third phase is also known as "Golden era of anti microbial therapy", was unshared by Domagk in 1935 by demonstrating the therapeutic effect of prontosil, a sulphonamide dye, in pyrogenic infection. It was soon realised that the active moiety was para -amino benzene sulphonamide, and the dye part is not essential. Later sulpha pyridine was synthesised and which was the first sulphonamide to be marketed in 1938.[5]

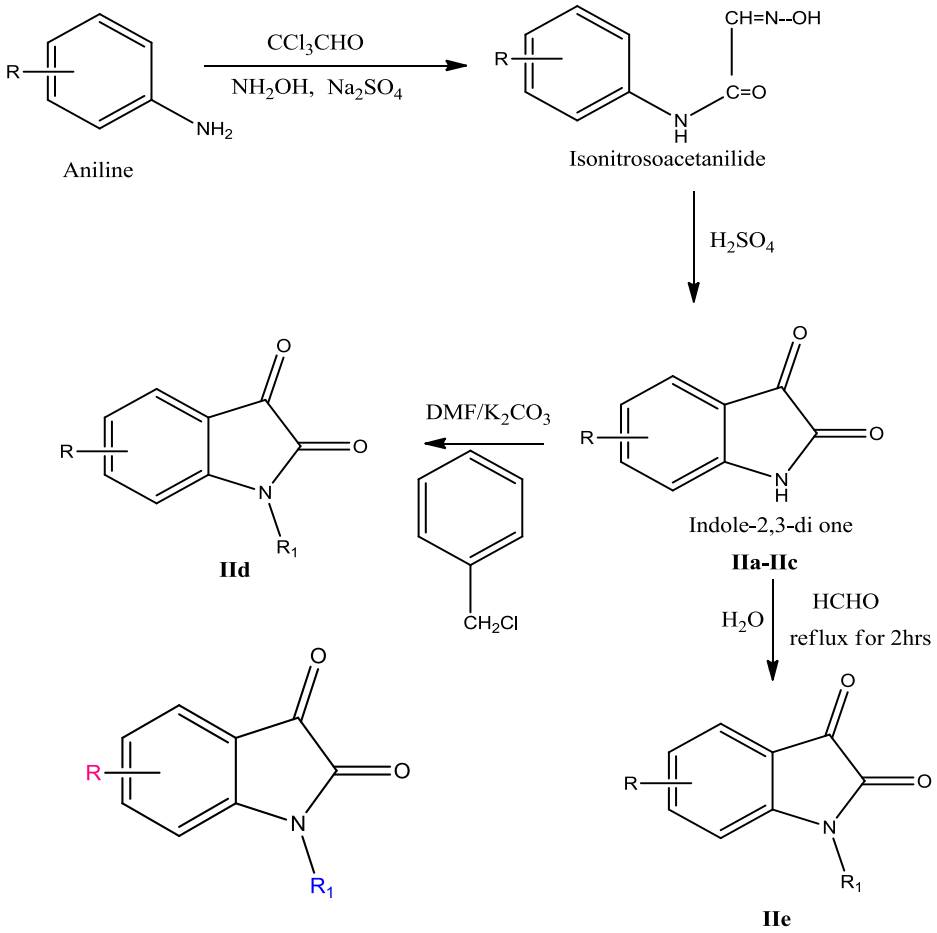
Non-steroidal anti-inflammatory drugs (NSAIDs) have a wide clinical use for the treatment of inflammatory and painful conditions including rheumatoid arthritis, soft tissue and oral cavity lesions, respiratory tract infections and fever. The two isoforms of cyclooxygenase (COX) are poorly distinguishable by most of the classical NSAIDs and these agents actually inhibit COX-1 extensively, besides COX-2, leading to gastrointestinal injury, suppression of TXA2 formation and platelet aggregation. The combination of these interactions is probably the reason for gastrointestinal bleeding as the most serious complication of these drugs. Some evidences suggest that the hydrazone moiety present in some compounds possess a pharmacophoric character for the inhibition of COX.

EXPERIMENTAL SECTION

Materials

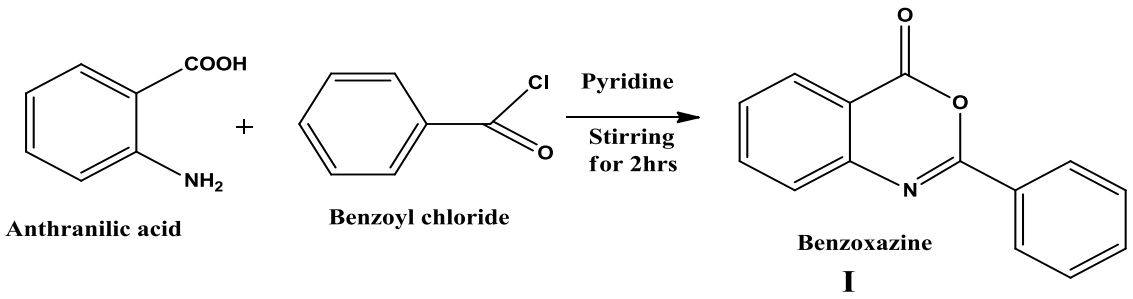
The chemicals used in the synthetic work were anthranilicacid, pyridine, benzoylchloride, 5% sodiumbicarbonate, hydrazine hydrate, veratraldehyde, salicylaldehyde, N,N-Dimethyl formamide, isatin, 3-Acetyl coumarin, 4-Methyl benzaldehyde, dimethyl amino benzaldehyde, furan-2- aldehyde, hydroxy methyl isatin, vanillin, anisaldehyde, alcohol, chloroform, methanol, silicagel (60-120 mesh) were purchased from SD Fine chemicals and Aldrich. All the the solvents used were AR grades were obtained from E.Merck, Mumbai and Sd fine chem., Mumbai. The reagents were obtained from Fluka and E.Merck, Loba chemie.

METHODOLOGY

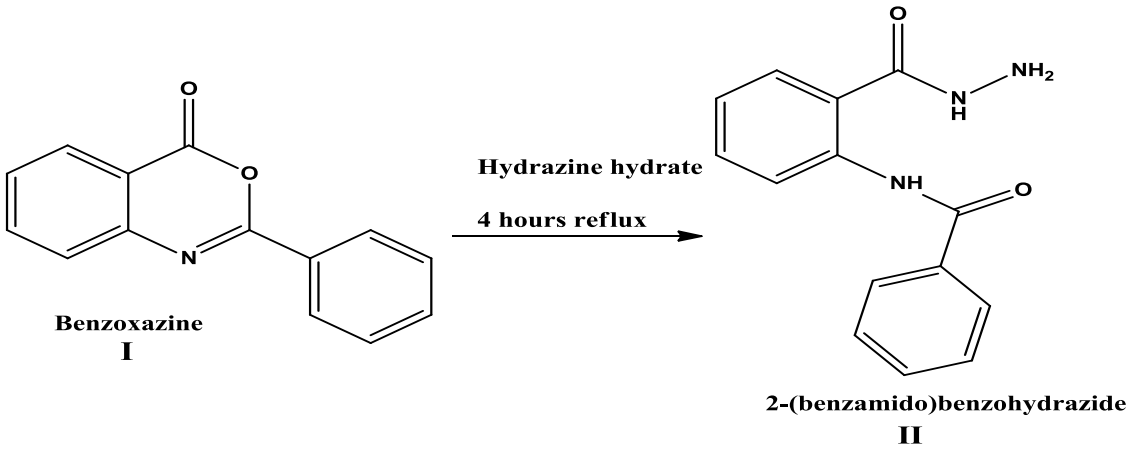


CODE	R_1	R_5
II a	H	H
II b	H	Cl
II c	H	Br
II d	CH_2-C_6H_5	H
II e	CH_2OH	H

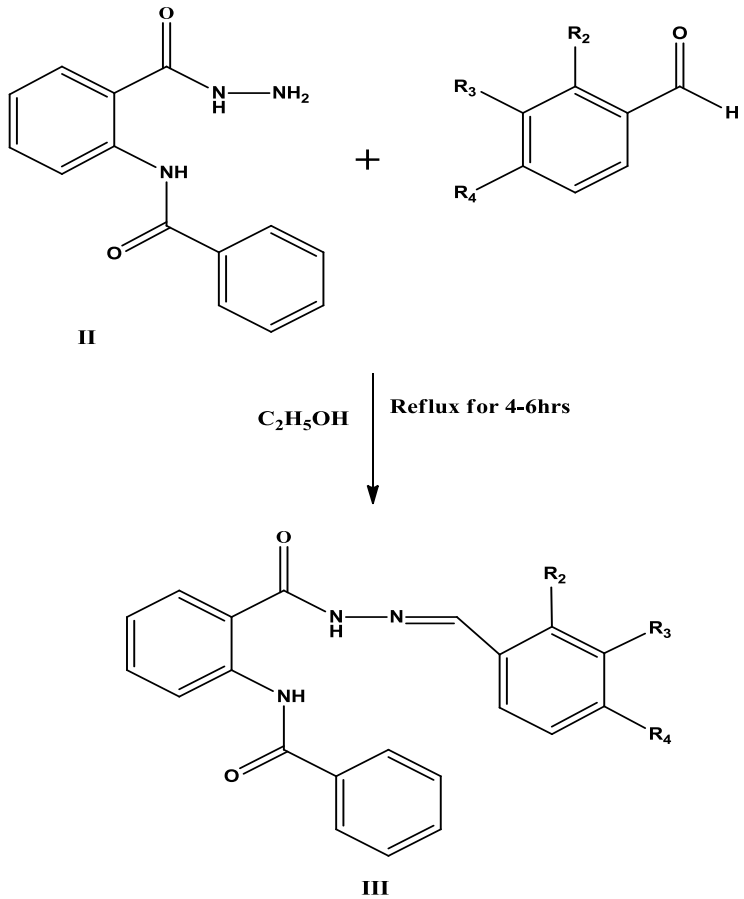
Scheme-I: Preparation of indole-2,3- dione and its derivatives.[68,69]



SCHEME-II: Step-I: Synthesis of benzoxazine from Anthranilicacid.[70]

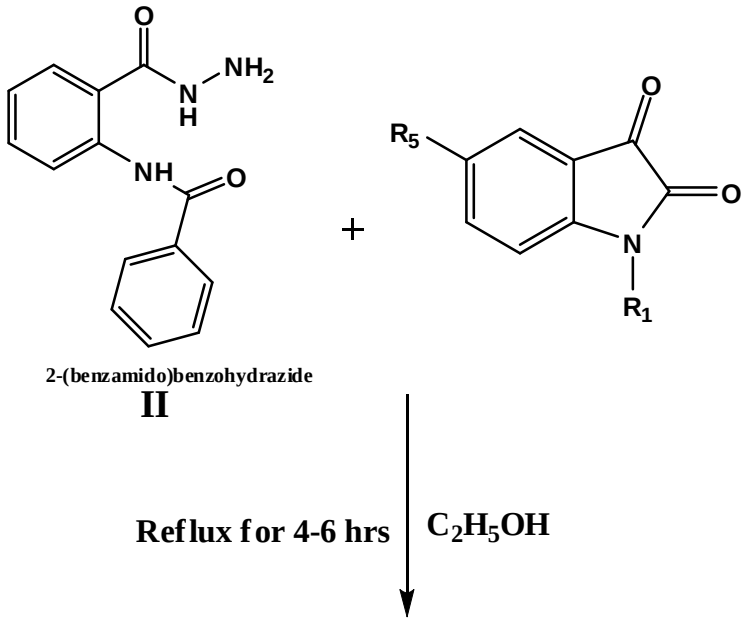


Step-II: Synthesis of 2-(benzamido)benzohydrazide.



CODE	R_2	R_3	R_4
IIIa	H	H	CH_3
IIIb	H	H	$N(CH_3)_2$
IIIc	H	OCH_3	OCH_3
IIId	H	OCH_3	OH
IIIe	H	H	OCH_3
IIIf	OH	H	H

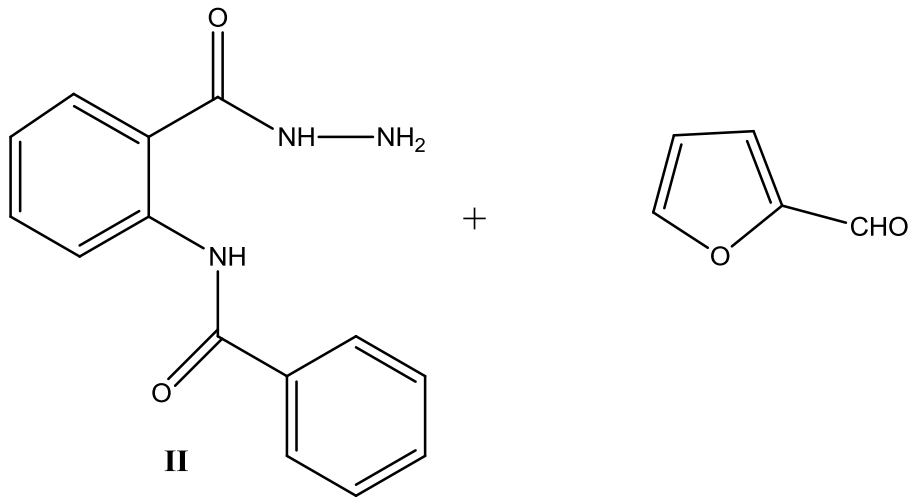
SCHEME-III: Preparation of aromatic hydrazone derivatives.[71]



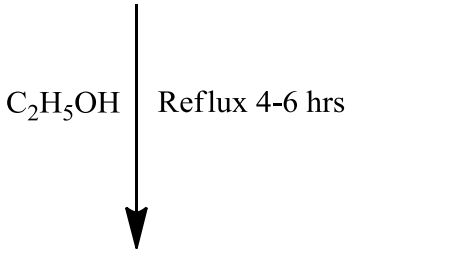
IIIg- IIIk

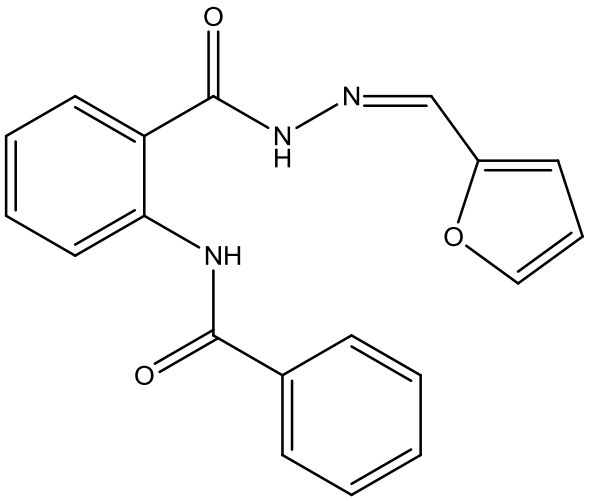
CODE	R_1	R_5
IIIg	H	H
IIIh	H	Cl
IIIi	H	Br
IIIj	CH_2-C_6H_5	H
IIIk	CH_2OH	H

SCHEME- III: Preparation of heterocyclic hydrazone derivatives.



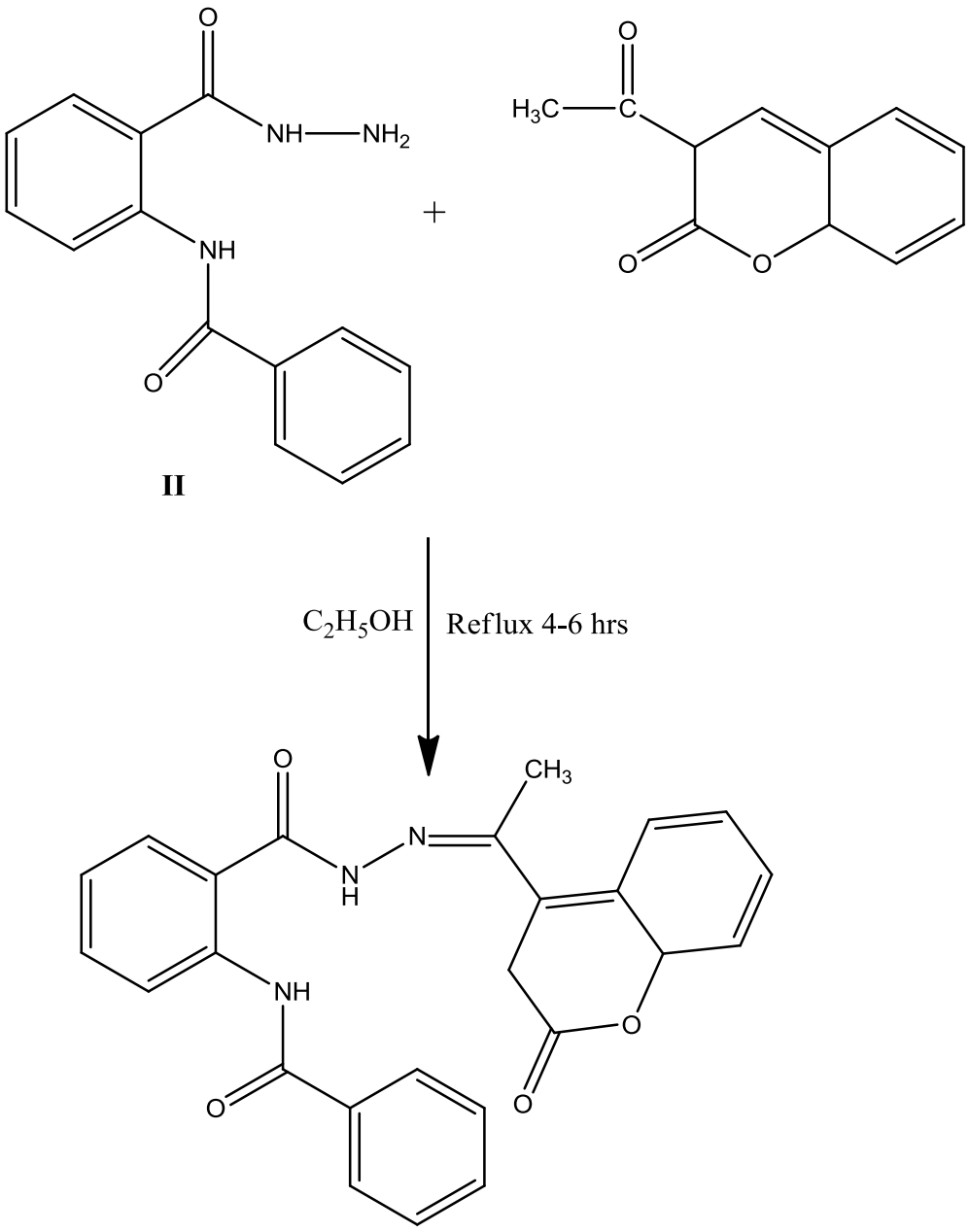
II





IIII

SCHEME-III: Preparation of heterocyclic derivatives.[71]



IIIm

SCHEME-III: Preparation of heterocyclic derivatives.[71]

5. EXPERIMENTAL INVESTIGATIONS

The identification and characterization of the prepared compounds were carried out by the following procedure.

- Melting Point
- Thin layer chromatography (TLC)
- FT-Infrared Spectroscopy (FT-IR)
- Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR & ^{13}C-NMR)

❖ Mass Spectroscopy (m/z)

➢ **Melting Point Determination**

The melting points of the organic compounds were determined by open capillary tube and are uncorrected. Melting point is a valuable criterion of purity for an organic compound, as a pure crystals is having definite and sharp melting point. The purity should not be assumed but must be established by observation of any changes in the melting point when the compound is subjected to purification by recrystallization.

➢ **Thin Layer Chromatography**

Thin layer chromatography is an important technique to identify the formulation of new compounds and also to determine the purity of the compounds. The R_f value is the characteristic for each compound.

Purity of the compounds was checked by thin layer chromatography using silica gel G as stationary phase and various combinations of ethyl acetate: cyclohexane as mobile phase. The spots resolved were visualized by using iodine chamber and UV chamber.

➢ **Fourier- Transformer-Infrared Spectroscopy (FT-IR)**

FT-IR can be routinely used to identify the functional groups and for quality control of raw materials finished products. Jasco 410 FT-IR spectrometer used to record IR spectra using KBr disc method.

➢ **Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR & ^{13}C-NMR)**

^{1}H- NMR and ^{13}C-NMR spectra were measured in d_6-DMSOand $CDCl_3$ on a Bruker Ultraspec 500MHz/ AMX400MHz spectrometer. The chemical shifts were reported against TMS.

➢ **Mass Spectroscopy (m/z)**

For recording the FAB-Mass Spectra JEOL SX 102/Da-600 mass spectrometer with m-NBA matrix.

The experimental work comprises of:

Scheme-I: Method for preparation of indole-2,3-dione (Isatin)[68,69]

Step-a: Method for preparation of isonitrosoacetanilide from aniline

In a 250ml round bottomed flask are placed 9gm (0.05M) of chloral hydrate and 120ml of water is added to this solution then about 13gm, of crystallized sodium sulphate, a solution of 4.3ml (0.05M) of aniline in 30ml of water to which 4.3ml (0.052M) of concentrated hydrochloric acid has been added to dissolve the amine and finally, a solution of 11gm (0.158M) hydroxylamine hydrochloride in 50ml of water. The flask is heated over a mantle heater so that vigorous boiling begins in about 40-45mins. After 1-2 min of vigorous boiling the reaction complete. During the heating period, some crystals of isonitrosoacetanilide separate. On cooling the solution in cold water the remainder crystallizes, is filtered with suction and air dried.

Step-b: Method for preparation of isatin from isonitrosoacetanilide

32.6 ml of concentrated sulphuric acid is warmed to 50°C in a 100ml R.B.F fitted with an efficient mechanical stirrer and 7.5gm of (0.046M) of dry isonitrosoacetanilide is added to such a rate as to keep the temperature between 60-70^{o}C but no higher. External cooling should be applied at this stage so that the reaction can be carried out more rapidly. After the addition of the isonotrosoacetanilide compound is finished, the solution is heated to 80°C and kept at this temperature for about ten minutes to complete the reaction. Then the reaction mixture is cooled to room temperature and poured to ten to twelve times its volume of cracked ice. After standing for about one and half hour, the isatin is filtered with suction, washed several times to cold water to remove the sulphuric acid and then dried in the air. For the purification three times its weight of glacial acetic acid was used as a result. Large brown red crystals which melts at 196-197^{o}C.

Step-c: Method for preparation of N-benzyl indole 2,3- dione from indole 2,3-dione (Isatin)

In the round bottomed flask take indole-2,3-dione (Isatin) 0.8gm (0.00337M) and equimolar quantity of benzyl chloride i.e 6.5ml (0.0037), mix with 20ml of DMF and to this mixture add 2gm of K_2CO_3. After gentle mixing of this reaction mixture, reflux for 2 hr, cool and pour to 100 ml of ice cold water. The resultant orange red ppt. collected wash with water and dried and recrystallized from acetonitrile.

Scheme-II

Step-I: Synthesis of 2-phenyl-3,1-benzoxazine-4-one[70]

Place a solution of anthranillic acid (0.1M), pyridine (60 ml), benzoyl chloride (0.2M) was added. The mixture was stirred for 2 hrs followed by treatment with 5% sodium bicarbonate (15ml). The solid obtained was recrystallised from ethanol.

Step-II Synthesis of 2-(benzamido)benzohydrazide

Place a mixture of above product (0.05M) and hydrazine hydrate (0.05M) in ethanol was refluxed for 3hrs and cooled. The separated solid was recrystallized from ethanol.

(or)

A mixture of first step product (0.01M) and hydrazine hydrate (0.01M), in dry pyridine (50ml) was heated under reflux for 3hrs. Subsequently mixture was poured into water (few drops of HCl). Thus seperated solid was filtered, washed, dried and recrystalized with ethanol.

Scheme-III: Preparation of hydrazone derivatives[71]

Place a mixture of 3-amino 2-phenyl hydrazone-4-3(*H*)-one (0.01M), the appropriate heterocyclic aldehyde or Aromatic aldehyde (0.01M) & ethanol (20ml) was refluxed for 4-6 hrs. The resulting mixture was cooled and poured in to ice water. The separated solid was filtered, washed with water and recrystallised from ethanol.

8. RESULTS AND DISCUSSION

8.1. Chemistry

Results are summarized in tables and schemes I to III show the details of the synthetic strategy adopted for the synthesis of Hydrazone derivatives. Hydrazone derivatives are prepared by reaction of different aromatic and heterocyclic aldehydes. All the synthesized Hydrazone derivatives were recrystalized by ethanol and characterised on the basis of physical and spectral data.

All the synthesised compounds were purified by successive recrystalization using ethanol. The purity was checked by performing TLC. The structures of the synthesised compounds were determined on the basis of their FT-IR, ^{1}H-NMR, ^{13}C-NMR and MASS spectral data. Mobile phase used for the column chromatography is $CHCl_3$-CH_3OH solvent mixture.

8.2. Spectral analysis

I.R Spectra of N-(2-(2-(4-methylbenzyl)hydrazinecarbonyl)phenyl)benzamide showed bands at 3336 for NH, 3298 for NH, 3064 for CH-Ar, 2975 for CH, 1528 for C=C.^{1}H-NMR spectra there are 21 resonance peaks at 10.06-7.34 δ ppm respectively. In Mass spectra molecular ion peak was found at 358, this confirms the authenticity of compound.

In case of 2-(benzamido)-N'-(1-benzyl-2,3,3a,7a-tetrahydro-2-oxo-1*H*-indol-3-yl) benzohydrazide showed I.R bands at 3306 for NH, 3065 for CH-Ar, 1661 for C=O, 1470 for C=C. In ^{1}H-NMR there are 25 well-resolved resonance peaks at field at (8.02-1.04), δ ppm respectively. In case of ^{13}C-NMR there are 20 well-resolved resonance peaks at (161.14-38.9), δ ppm respectively. MASS Spectra of the compound shows the base peak at 356.3 due to the loss of benzamide group. This confirms the authenticity of compound.

In 2-(benzamido)-N'-((furan-2-yl)methylene) benzohydrazide showed I.R bands at 3384 for NH, 3269 for NH, 3042 for CH-Ar, 1698 for C=N, 1664 for C=O. In case of ^{1}H-NMR there are 18 well-resolved resonance peak at (12.07-6.66), δ ppm respectively. In case of ^{13}C-NMR, in aromatic region shows 21 well resonance peaks (164-38.91) δppmrespectively. MASS Spectra of the compound shows the base peak at 332.2This confirms the authenticity of compound respectively.

In case of N-(2-(2-(4-(dimethyl amino)benzyl)hydrazine carbonyl)phenyl)benzamideshowed I.R Spectra of 3318 for NH, 3226 for NH, 3058 for CH-Ar, 2984 for CH, 1681 for C=O, 1545 for C=C. In case^{1}H-NMR 16 well-resolved resonance peak at 9.94-7.22δ ppm respectively. In case of MASS spectra of the compound shows the base peak at 387 this confirms the authenticity of compound.

In case of N-(2-(2-(3,4-dimethoxybenzyl)hydrazinecarbonyl)phenyl)benzamide showed I.R bands at 3336 for NH, 3212 for NH, 3060 for CH-Ar, 2997 for CH, 1764 for C=N1676 for C=O, 1512 for C=C. In case ^{1}H-NMR well-resolved resonance peak at field at 10.12-7.24δ ppm respectively. in case of ^{13}C-NMR 14 well-resolved resonance peak at field at 166.48-112.44δ ppm respectively. in case of MASS spectraof the compound shows the base peak 404this confirms the authenticity of compound.

In case of N-(2-(2-(2-oxoindolin-3-yl)hydrazine carbonyl)phenyl benzamideshowed I.R bands at 3388 for NH, 3249 for NH 3066 for CH-Ar, 1694 for C=N, 1654for C=O1601 for

NH, C=C for 1534, In case of ^{1}H-NMR 18 well-resolved resonance peak at field at 10.12-7.04δ ppm respectively. In case of MASS spectra of the compound shows the base peak 385this confirms the authenticity of compound.

In case of 2-(benzamido)-N'-(1-(4a,8a-dihydro-2-oxo-2H-chromen-3-yl)ethylidene) benzohydrazide showed I.R bands at 3306 for NH, 3216 for NH, 3071 for CH-Ar, 1660 for C=O, 1610 for C=N, 1561 for C=C. In case of ^{1}H-NMR15 well-resolved resonance peak at field at 8.04- 5.84δ ppm respectively, In case of MASS spectra of the compound shows the base peak 428This confirms the authenticity of compound.

In case of N-(2-(2-(2-hydroxy benzyl)hydrazine carbonyl)phenyl)benzamide showed I.R bands at 3562 for OH, 3366 for NH, 3226 for NH, 3088 for CH-Ar, 2973 for CH, 1680 for C=O, 1585 for C=C. In case of ^{1}H-NMR 15 well-resolved resonance peak at field at 8.15-7.12δ ppm respectively. In case of ^{13}C-NMR 16 well-resolved resonance peak at field at 169.12-111.18δ ppm respectively. In case of MASS spectra of the compound shows the base peak 360. This confirms the authenticity of compound.

8.3. Biological Activity and Discussion

Antibacterial activity

The compounds were evaluated for its antibacterial activity by cup- plate method. Results are summarized in **table-4** respectively, 10 compounds were tested on various strains of microbes, bacteria like *Klebsiella pneumoniae, Salmonella paratyphi, Eischeresia coli* and *Bacillus substilis, Staphylococcus Aureus.*

Significant antibacterial activity was observed for, against the microorganisms like *S.paratyphi, E.coli, B.substilis, K.pneumoniae*. The zone of inhibition of test compounds compared with the zone of inhibition with standard drug Streptomycin. **IIIc, IIIe** compounds showed significant activity against *K.pneumoniae*. **IIIg** compound showed significant activity against *B.subtilis*, **IIIl** compound showed activity against *E.coli*., **IIIf** compound showed moderate activity against *S.paratyphi, E.coli, B.substilis, K.pneumoniae,* However all of the compounds failed to show significant antibacterial activity againststrains of microbes, bacteria like *Klebsiella pneumoniae, Salmonella paratyphi, Escheria coli* and *Bacillus substilis.*

Antifungal activity

The compounds were evaluated for its antifungal activity by cup- plate method. Results are summarized in **table-5** respectively, 10 compounds were tested on various strains of fungal sporeslike *Pencillin notatum, Aspergillus clavatus, Aspergillus nigrum, Colliotricum coffeanum*. The significant antifungal activity was observed for the most of the hydrazonederivatives by cup-plate method.

The zone of test compounds compared with the zone of inhibition with standard drug Griseofulvin. **IIIa, IIIe** compounds showed significant activity against *Aspergillus nigrum.* **IIIb, IIId, IIIl** compounds showed activity against *Aspergillus clavatus,* **IIIc** compound showed significant activity against *Pencilium notatum*, **IIId, IIIg, IIIh** compounds showed significant activity against *Colletotrichem coffeanum.* all of the compounds failed to showed significant antifungal activity against fungal spores likes *Pencillin notatum.*

The results of the antibacterial and antifungal screening clearly demonstrate the antibacterial and antifungal activity of the hydrazone derivatives against the different microorganisms and fungal spores.

Analgesic activity

Acetic acid Induced Writhing Test (Chemical Stimulation)

The analgesic activity of the samples was evaluated using acetic acid induced writhing method in rats. In this method, acetic acid is administered intraperitoneally to the experimental animals to create pain sensation. As a positive control, any standard NSAID drug can be used. In the present study Diclofenac sodium was used to serve thepurpose. Accordingly, two half-writhing were taken as one full writhing. The number of writhes ineach treated group was compared to that of a control group while Diclofenac sodium (100mg/kg) was used as a reference standard (positive control).

Results are summarized in **table-6** respectively, 3 compounds were tested for analgesic activity by Acetic acid induced method. In accordance with the data obtained from analgesic activity, among Hydrazone derivatives **IIIm** showed significant analgesic activity. The activity was determined by comparing with standard Diclofenac (100mg/kg) was used as a reference (positive control). All the values were expressed as Mean ± S.E.M, N=3, statistical analysis was done by one way ANOVA using Graph Pad Prism 5. **IIIm** Compound showed

significant activity where as the **IIIl** compound showed moderate activity(P<0.01), **IIIa** compound showed mild activity(P <0.05).

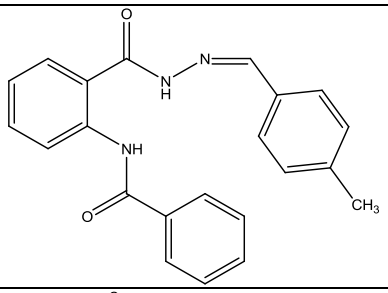
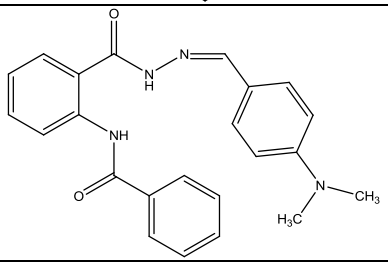
***In vitro* Cytotoxic activity**

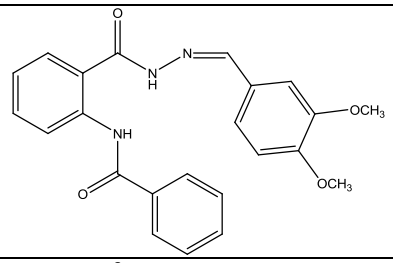
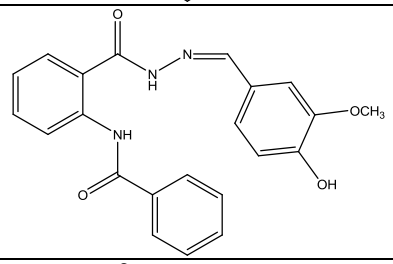
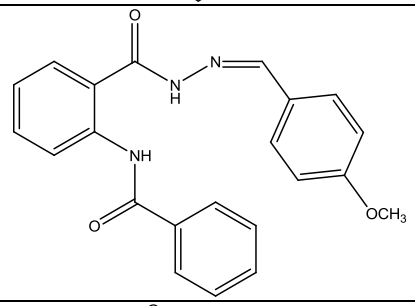
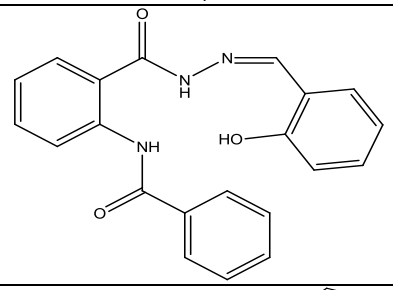
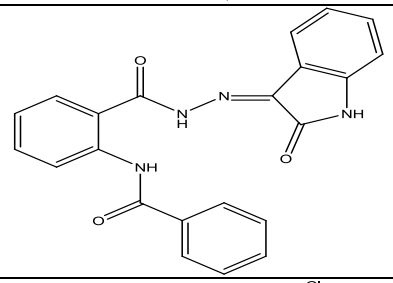
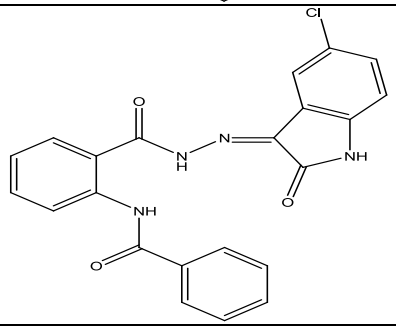
Murine leukemia L1210, human T-lymphocyte Molt 4/C8, and CEM cells were suspended at 300000-500000 cells/Ml of culture medium, and an amount of 100 µL of these cell suspensions was added to 200 µL micro-titer plate wells containing 100 µL of an appropriate dilution of the test compounds. After 2 days (L1210) or 3 days (Molt 4/C8 and CEM) of incubation at 37°C, the cell number was determined using a Coulter counter. The 50% cytostatic concentration (IC_{50}) was defined as the compound concentration required to inhibit cell proliferation by 50%.

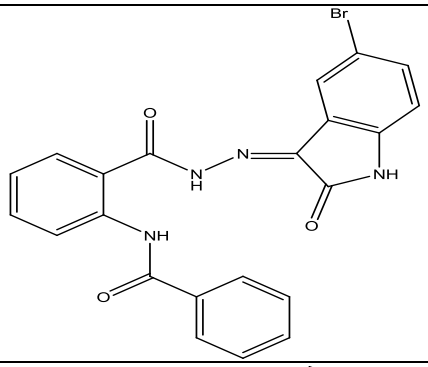
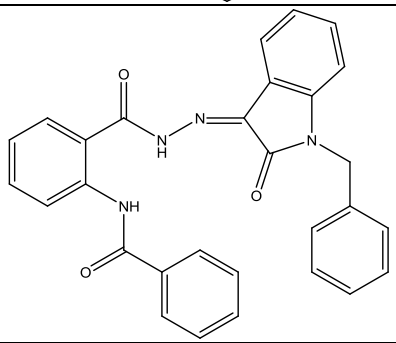
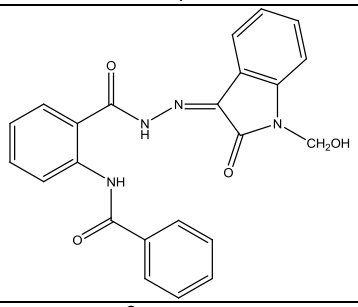
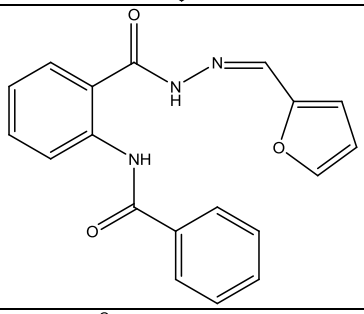
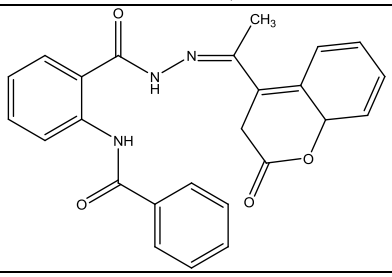
Results are summarized in **table-7** respectively, 10 compounds, were tested for *in-vitro* cytotoxic activity against human cancer cell lines CEM, L1210, Molt 4/C8, HL60, Molt 4/C8 and murine tumor cell line, BEL7402. *In vitro* evaluation of these hydrazone derivatives revealed cytotoxic activity from 1.2 to > 40µm against CEM, 23 to > 230µm against < L1210, 15 to >130µm against Molt 4/C8, 12 to >200µm against HL60 & 12 to > 175 µm against BEL 7402 respectively. The compound **IIIb** showed significant cytotoxic activity against all the five cell lines tested in the region of 9, 23, 33, 26, 17µm for CEM, L1210, Molt 4/C8, HL60 & BEL 7402 respectively. These compounds are compared with standarad drug Melphalan.

6. EXPERIMENTAL RESULTS

6.1. Table 1: Structures and IUPAC names of Hydrazone derivatives.

Code	Structure	IUPAC Name
IIIa		**N-(2-(2-(4-methylbenzyl)hydrazinecarbonyl) phenyl)benzamide**
IIIb		**N-(2-(2-(4-(dimethyl amino)benzyl)hydrazine carbonyl)phenyl)benzamide**

IIIc		**N-(2-(2-(3,4-dimethoxybenzyl) hydrazinecarbonyl) phenyl)benzamide**
IIId		**N-(2-(2-(4-hydroxyl-3-methoxybenzyl)hydrazinecarbonyl)phenyl) benzamide**
IIIe		**N-(2-(2-(4-methoxy benzyl)hydrazinecarbonyl) phenyl)benzamide**
IIIf		**N-(2-(2-(2-hydroxy benzyl)hydrazine carbonyl)phenyl) benzamide**
IIIg		**N-(2-(2-(2-oxoindolin-3-yl)hydrazine carbonyl)phenyl benzamide**
IIIh		**N-(2-(2-(5-chloro-2-oxoindolin-3-ylidene) hydrazinecarbonyl) phenyl) benzamide**

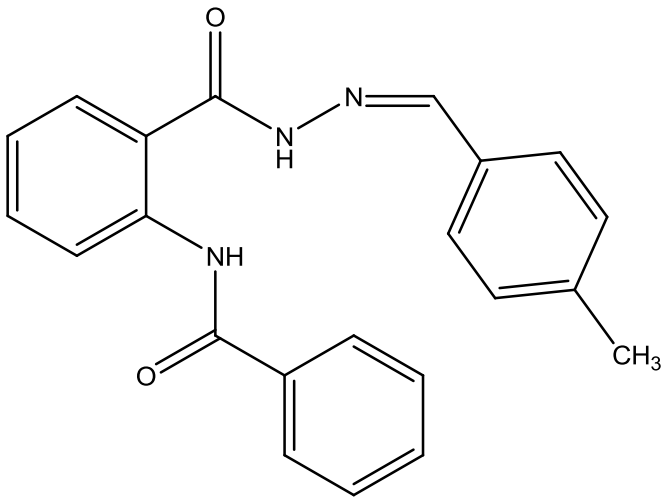
IIIi		**N-(2-(2-(5-bromo-2-oxoindolin-3ylidene)hydrazine carbonyl) phenyl) benzamide**
IIIj		**N-(2-(2-(1-benzyl-2-oxoindolin-3-yl)methyl)hydrazine carbonyl)phenyl)benzamide**
IIIk		**Z)-N-(2-(2-(1-(hydroxylmethyl)-2-oxoindolin-ylidene) hydrazine carbonyl) phenyl)benzamide**
III l		**2-(benzamido)-N'-((furan-2-yl)methylene) benzohydrazide**
IIIm		**2-(benzamido)-N'-(1-(4a,8a-dihydro-2-oxo-2H-chromen-3-yl)ethylidene)benzohydrazide**

6.2. Table no. 2: Physical characterization of Hydrazone derivatives.

Code	Nature of crystals	Mol.Wt	Mol.Formula	%Yield	Melting point
IIIa	Cream crystals	357	$C_{22}H_{19}N_3O_2$	87.6	210-212^{0}C
IIIb	White crystals	386	$C_{23}H_{22}N_4O_2$	83.6	238-240^{0}C
IIIc	Cream crystals	403	$C_{23}H_{21}N_3O_4$	86.5	128-131^{0}C
IIId	Cream crystals	389	$C_{24}H_{19}N_3O_4$	84.8	228-230^{0}C
IIIe	White crystals	373	$C_{22}H_{19}N_3O_3$	87	208-212^{0}C
IIIf	Cream crystals	359	$C_{21}H_{17}N_3O_2$	82	222-224^{0}C
IIIg	Yellow crystals	386	$C_{22}H_{18}N_4O_3$	80	260-263^{0}C
IIIh	Red amorphous	418	$C_{22}H_{15}N_4O_3Cl$	81	292-294^{O}C
IIIi	Yellow amorphous	463	$C_{22}H_{15}N_4O_3Br$	86	279-282^{O}C
III j	White crystals	474	$C_{29}H_{22}N_4O_3$	85.3	159-162^{o}C
IIIk	Pale yellow crystals	416	$C_{23}H_{20}N_4O_4$	83	246-249^{0}C
III l	Cream crystals	333	$C_{19}H_{15}N_3O_3$	90	198-201^{0}C
IIIm	Pale yellow crystals	427	$C_{25}H_{21}N_3O_4$	78.2	172-173^{0}C

6.3. Analytical and Spectral data for the following compounds

IIIa) N-(2-(2-(4-methylbenzyl)hydrazinecarbonyl)phenyl)benzamide



Molecular formula : $C_{22}H_{19}N_3O_2$

Molecular weight : 357

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

R_f value : 0.92

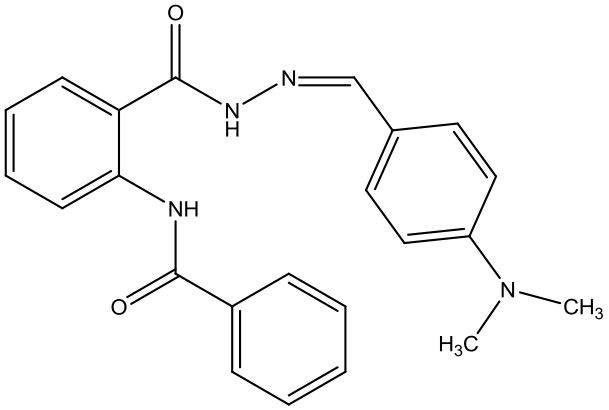
I.R Spectrum : 3336 (NH), 3298 (NH), 3064 (CH-Ar), 2975 (CH), 1669 1528 (C=C)

^{1}H-NMR : 10.06 (1H, CO-NH), 9.84 (1H, NH-CO), 8.38 (1H, CH=N), 8.04-7. 94 (3H), 7.88-7.65 (5H), 7.38 (2H), 7.34 (1H), 7.16-7.04 (2H), 2.32-2.28 (3H, CH_3)

^{13}C-NMR : 165.54 (1C, CO-NH), 164.28 (1C, NH-CO), 139.82 (1C, (C=N), 138.9 (1C, C-NH), 134.52-113.68 (17C, Ar-CH), 228 (1C, CH_3).

MASS : 358 (M+1)

IIIb) N-(2-(2-(4-(dimethyl amino)benzyl)hydrazine carbonyl)phenyl)benzamide



Molecular formula: $C_{23}H_{22}N_4O_2$

Molecular weight: 386

Solubility: Ethanol, Chloroform, DMSO

Mobile phase: ethanol: chloroform

R_f value: 0.47

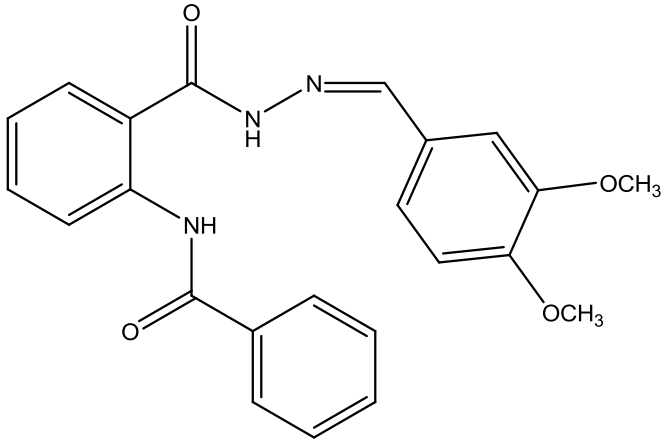
I.R Spectrum: 3318 (NH), 3226 (NH), 3058 (CH-Ar), 2984 (CH), 1681 (C=O), 1545 (C=C)

^{1}H-NMR: 9.94 (1H, CO-NH), 9.86 (1H, NH-CO), 8.52 (1H, CH=N), 8.1-7.92 (3H), 7.88-7.74 (2H), 7.52-7.36 (4H), 7.28-7.22 (2H), 7.1-6.98 (2H), 3.14-2.98 (6H, N-$(CH_3)_2$)

^{13}C-NMR: 168.42 (1C, CO-NH), 166. 98 (NH-CO), 146.24 (1C, CH=N), 139.88 (1C, C-NH), 132.42-112.68 (17C, Ar-CH), 43.41-42.84 (2C, N-$(CH_3)_2$)

MASS: 387 (M+1)

IIIc) N-(2-(2-(3,4-dimethoxybenzyl)hydrazinecarbonyl)phenyl)benzamide



Molecular formula : $C_{23}H_{21}N_3O_4$

Molecular weight : 40

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

R_f value : 0.52

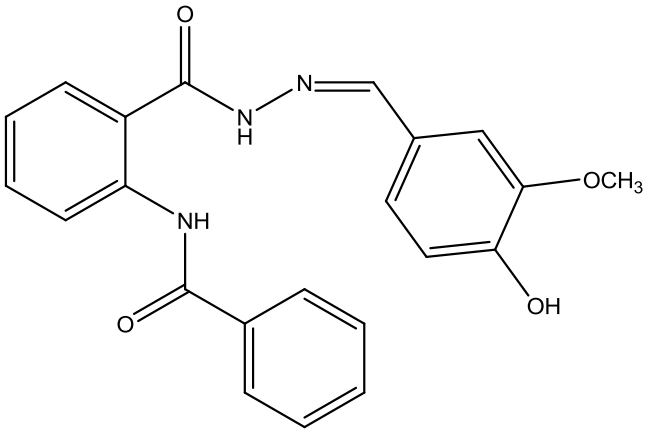
I.R Spectrum : 3336 (NH), 3212 (NH), 3060 (CH-Ar), 2997 (CH), 1764 (C=N)1676 (C=O), 1512 (C=C)

^{1}H-NMR : 10.12 (1H, CO-NH), 9.98 (NH-CO), 8.75 (1H, CH=N), 8.18-7.87(4H), 7.76-7.54 (3H), 7.48-7.42 (2H), 7.36 (1H), 7.24-7.12 (2H),3.82-3.78 (6H, di-OCH_3)

^{13}C-NMR : 166.48 (1C, CO-NH), 165.62 (1C, NH-CO), 153.46-151.82 (2C,C-O), 146.88 (1C, CH=N), 138.61-112.44 (16C, Ar-CH), 58.64-55.48 (2C, di-OCH_3).

MASS : 404 (M+1)

IIId) N-(2-(2-(4-hydroxyl-3-methoxybenzyl)hydrazinecarbonyl)phenyl) benzamide



Molecular formula : $C_{24}H_{19}N_3O_4$

Molecular weight : 389

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

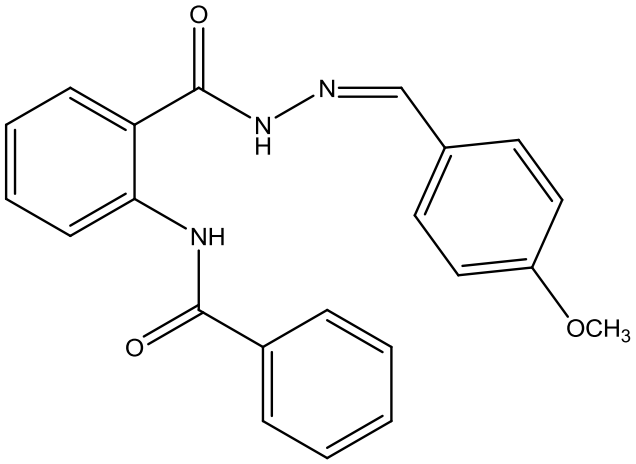
R_f value : 0.61

I.R Spectrum : 3585 (OH), 3317 (NH), 3244 (NH), 3068 (CH-Ar), 2982 (CH),1668 (C=O), 1574 (C=C)

^{1}H-NMR : 10.22 (1H, CO-NH), 9.82 (1H, NH-CO), 8.66 (1H, CH=N), 8.16-8.02 (4H), 7.98-7.76 (3H), 7.62-7.44 (3H), 7.16-6.98 (2H), 5.18(1H, OH), 3.76 (3H, OCH_3)

MASS : 390 (M+1)

IIIe) N-(2-(2-(4-methoxy benzyl)hydrazinecarbonyl)phenyl)benzamide



Molecular formula : $C_{22}H_{19}N_3O_3$

Molecular weight : 373

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

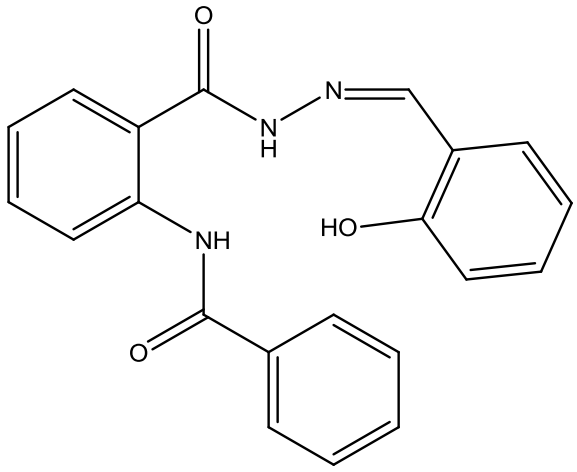
R_f value : 0.49

I.R Spectrum : 3338 (NH), 3212 (NH), 3036 (CH-Ar), 2986 (CH), 1664 (C=O),1598 (C=C)

^{1}H-NMR : 9.85 (1H, CO-NH), 9.64 (1H, NH-CO), 8.49 (1H, CH=N), 8.03-7.94 (5H), 7.88-7.62 (2H), 7.43-7.18 (3H), 7.08 (1H), 6.96-6.92(2H,), 3.81 (3H, OCH_3)

MASS : 374 (M+1)

IIIf) N-(2-(2-(2-hydroxy benzyl)hydrazine carbonyl)phenyl)benzamide



Molecular formula : $C_{21}H_{17}N_3O_3$

Molecular weight : 359

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

R_f value : 0.72

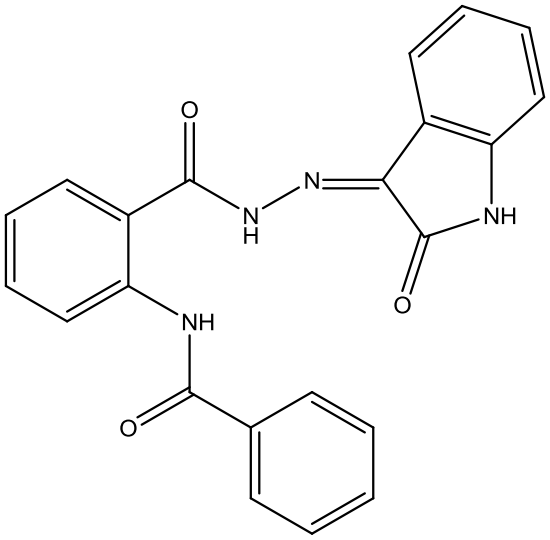
I.R Spectrum : 3285 (NH), 3204 (NH),3054 (CH-Ar), 1651 (C=O), 1527 (C=C)

^{1}H-NMR : 9.97 (1H, CO-NH), 9.68 (1H, NH-CO), 8.44 (1H, CH=N), 8.15- 7. 86 (4H), 7.72-7.68 3H), 7.44-7.32 (4H), 7.18-7.12 (2H), 5.28 (1H, OH)

^{13}C-NMR : 169.12 (1C, CO-NH), 166.98 (1C, NH-CO), 156.46 (1C, C-OH)138.28 (1C, CH=N), 137.64 (1C, C-NH), 131.25-111.18 (16C,Ar-CH)

MASS : 360 (M + 1)

IIIg) N-(2-(2-(2-oxoindolin-3-yl)hydrazine carbonyl)phenyl benzamide



Molecular formula : $C_{22}H_{16}N_4O_3$

Molecular weight : 384

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

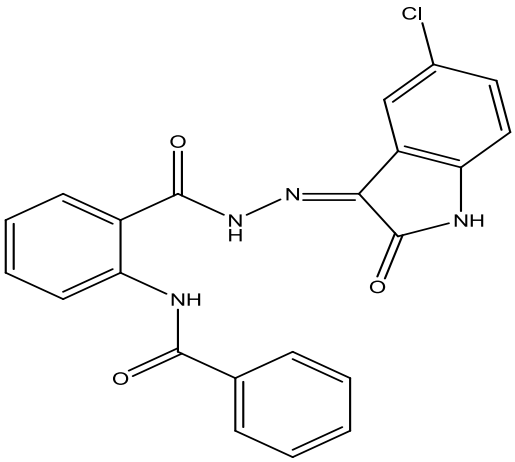
R_f value : 0.28

I.R Spectrum : 3388 (NH), 3249 (NH), 3066 (CH-Ar), 1694 (C=N), 1652 (C=O)1601 (NH), C=C (1534)

^{1}H-NMR : 10.12 (1H, CO-NH), 9.76 (1H, NH-CO) 8.24 (1H), 8.19 (1H), 7.96 (1H), 7.92 (1H), 7.86-7.82 (3H,), 7.7-7.56 (2H), 7.32-7.28(3H), 7.04-6.86 (2H)

MASS : 385 (M+1)

IIIh) N-(2-(2-(5-chloro-2-oxoindolin-3-ylidene)hydrazinecarbonyl) phenyl) benzamide



Molecular formula : $C_{22}H_{15}ClN_4O_3$

Molecular weight : 418

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

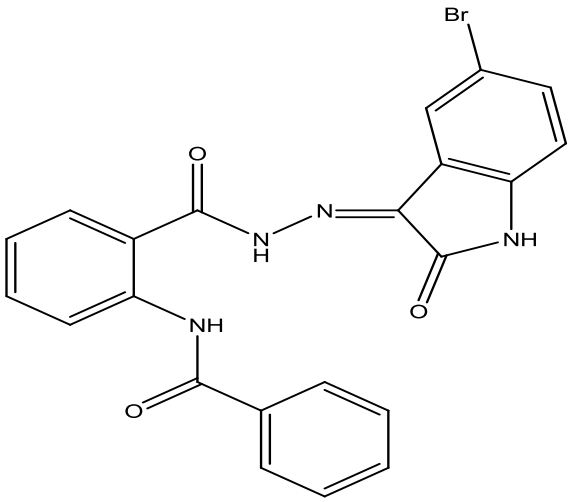
R_f value : 0.37

I.R Spectrum : 3332 (NH), 3288 (NH), 3015 (CH-Ar), 1685 (C=N), 1662 (C=O), 1604 (NH), C=C (1583)

^{1}H-NMR : 10.14 (1H, CO-NH), 10.02 (1H, NH-CO) 8.21 (1H), 8.04 (1H), 7.95 (1H), 7.8-7.71 (3H,), 7.65-7.44 (2H), 7.29-7.18 (3H), 7.02-6.88 (2H)

MASS : 418 (M+1)

IIIi) N-(2-(2-(5-bromo-2-oxoindolin-3ylidene)hydrazine carbonyl) phenyl) benzamide



Molecular formula : $C_{22}H_{15}N_4O_3Br$

Molecular weight : 463

Solubility : Ethanol, Chloroform, DMSO

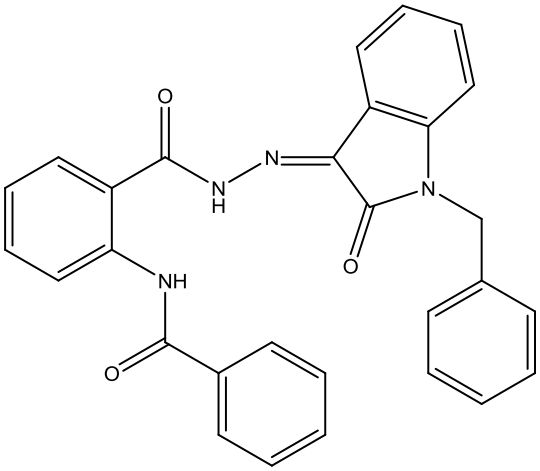
Mobile phase : ethanol: chloroform

R_f value : 0.73

^{1}H-NMR : 9.94 (1H, CO-NH), 9.67 (1H, NH-CO) 8.32 (1H), 8.08 (1H),7.96 (1H), 7.92-7.78 (3H,), 7.64-7.52 (2H), 7.22-7.08 (3H), 6.98-6.74 (2H)

MASS : 464 (M+1)

IIIj) N-(2-(2-(1-benzyl-2-oxoindolin-3-yl)methyl)hydrazine carbonyl)phenyl)benzamide



Molecular formula : $C_{29}H_{22}N_4O_3$

Molecular weight : 474

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

R_f value : 0.86

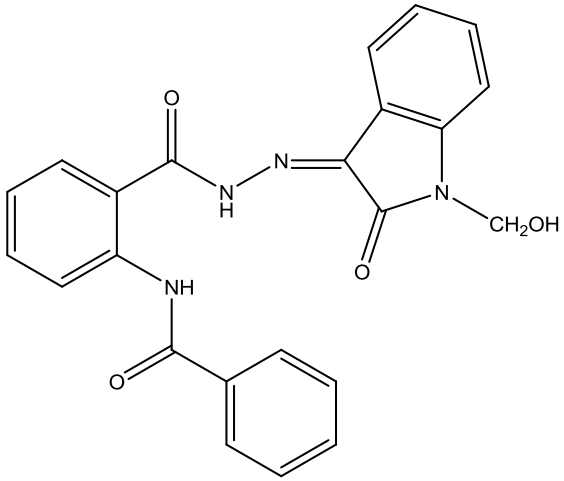
I.R Spectrum : 3306 (NH), 3216 (NH), 3065 (CH-Ar), 1661 (C=O), 1470 (C=C)

^{1}H-NMR : 8.209-8.207 (1H), 8.189-8.187 (1H), 7.96 (1H), 7.94 (1H), 7.87-7.80 (5H, Ar-CH), 7.72-7.70 (2H, Ar-CH), 7.58-7.54 (3H,Ar-CH),7.51-7.46 (4H, Ar-CH), 7.42-7.33 (2H, Ar-CH), 5.67 (2H, CH_2)

^{13}C-NMR : 161.14 (1C, CO-NH), 155.71 (1C, NH-CO), 146.69 (1C, C=O), 134.87-120.04 (24C, Ar-CH).

MASS : 475 (M+1), 497 (M+Na)

IIIk) (Z)-N-(2-(2-(1-(hydroxylmethyl)-2-oxoindolin-ylide ne)hy drazine carbonyl) phenyl)benzamide



Molecular formula : $C_{23}H_{18}N_4O_4$

Molecular weight : 414

Solubility : Ethanol, Chloroform, DMSO

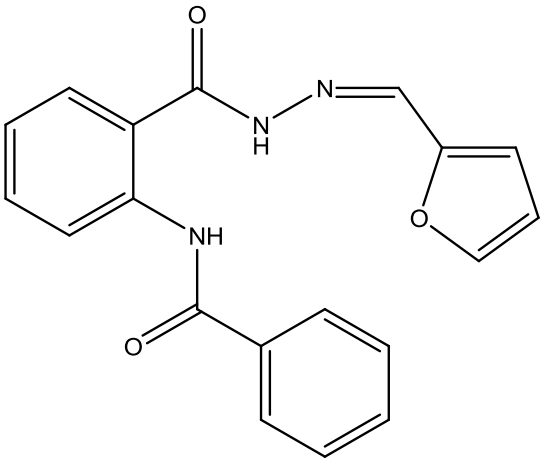
Mobile phase : ethanol: chloroform

R_f value : 0.58

^{1}H-NMR : 10.24 (1H, CO-NH), 10.04 (1H, NH-CO) 8.28 (1H), 8.10-7.98(4H), 7.87 (3H), 7.82 (1H), 7.66-7.52 (3H,), 7.26 (1H), 5.34 (2H, CH_2), 3.58 (1H, OH)

MASS : 415 (M+1)

IIIl)2-(benzamido)-N'-((furan-2-yl)methylene)benzohydrazide



Molecular formula : $C_{19}H_{15}N_3O_3$

Molecular weight : 333

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

R_f value : 0.59

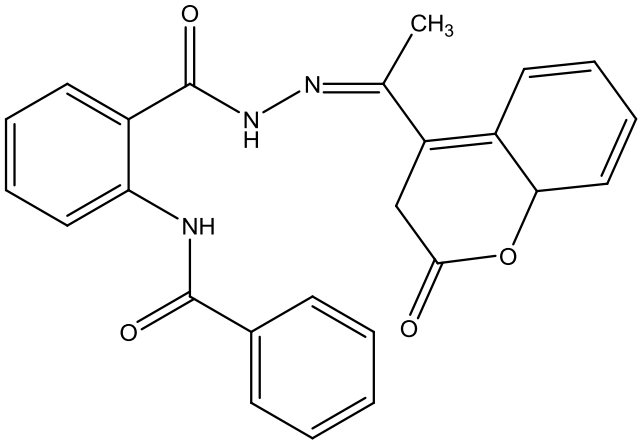
I.R Spectrum : 3384 (NH), 3269 (NH), 3042 (CH-Ar), 1698 (C=N), 1664 (C=O)

^{1}H-NMR : 12.07 (1H, CO-NH), 11.95 (1H, NH-CO), 8.59-8.57 (2H), 8.34(1H, CH=N), 7.98-7.88 (3H, Ar-CH), 7.65-7.58 (4H, Ar-CH),7.3-7.26 (1H, Ar-CH), 6.99 (1H, Ar-CH), 6.64 (1H, Ar-CH).

^{13}C-NMR : 164.88 (1C, CO-NH), 164.46 (1C, NH-CO), 149.2-145.49 (2C, C-O) 139.3 (1C, C-NH), 138.62 (1C, CH=N), 134.35-112.27(13C, Ar-CH).

MASS : 333 (M+1), 356 (M+Na)

IIIm) 2-(benzamido)-N'-(1-(4a,8a-dihydro-2-oxo-2H-chromen-3-yl) ethylidene) benzohydrazide



Molecular formula : $C_{25}H_{21}N_3O_4$

Molecular weight : 427

Solubility : Ethanol, Chloroform, DMSO

Mobile phase : ethanol: chloroform

R_f value : 0.63

I.R Spectrum : 3306 (NH), 3216 (NH), 3071 (CH-Ar), 1660 (C=O), 1610 (C=N), 1561 (C=C)

^{1}H-NMR : 10.67 (1H, CO-NH), 10.24 (1H, NH-CO), 8.04-8.01 (3H), 7.94-7.82 (3H), 7.6-7.53 (4H), 7.1-6.98 (2H), 5.84-5.82 (2H), 2.94 (2H), 2.14 (3H, CH_3)

MASS : 428 (M+1)

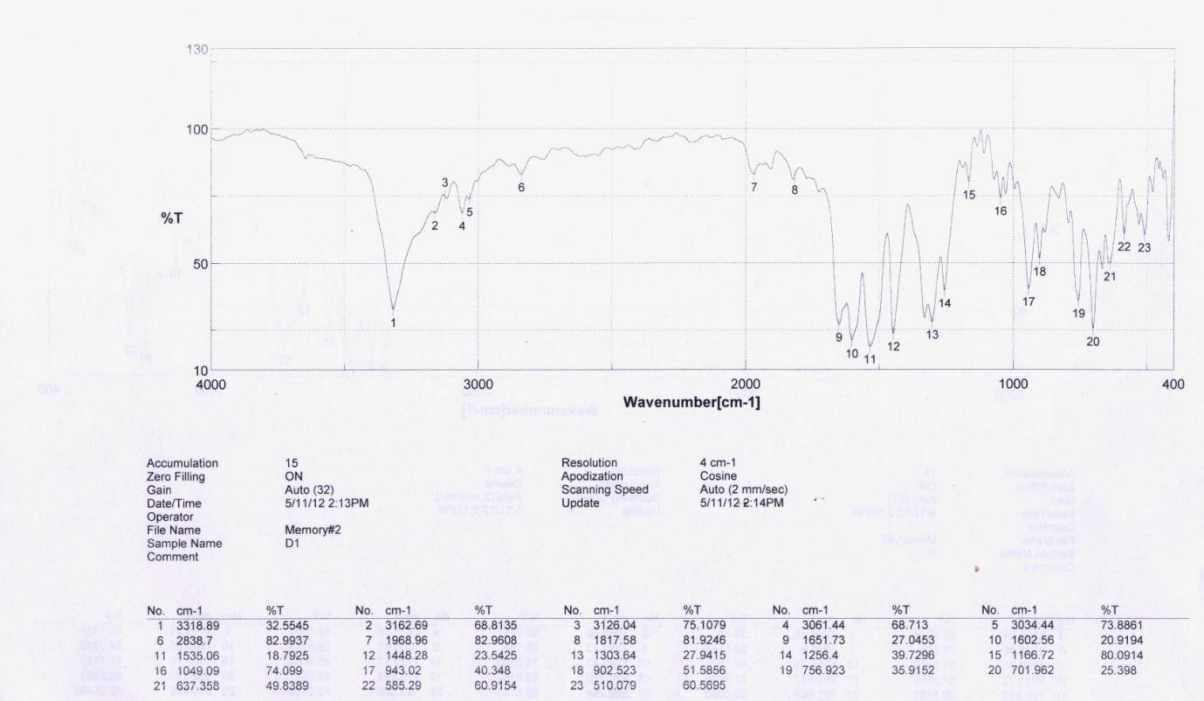


Figure 1: FT-IR Spectrum of 2-(benzamido)-*N'*-(1-benzyl-2,3,3a,7a-tetrahydro-2-oxo-1*H*-indol-3-yl)benzohydrazide.

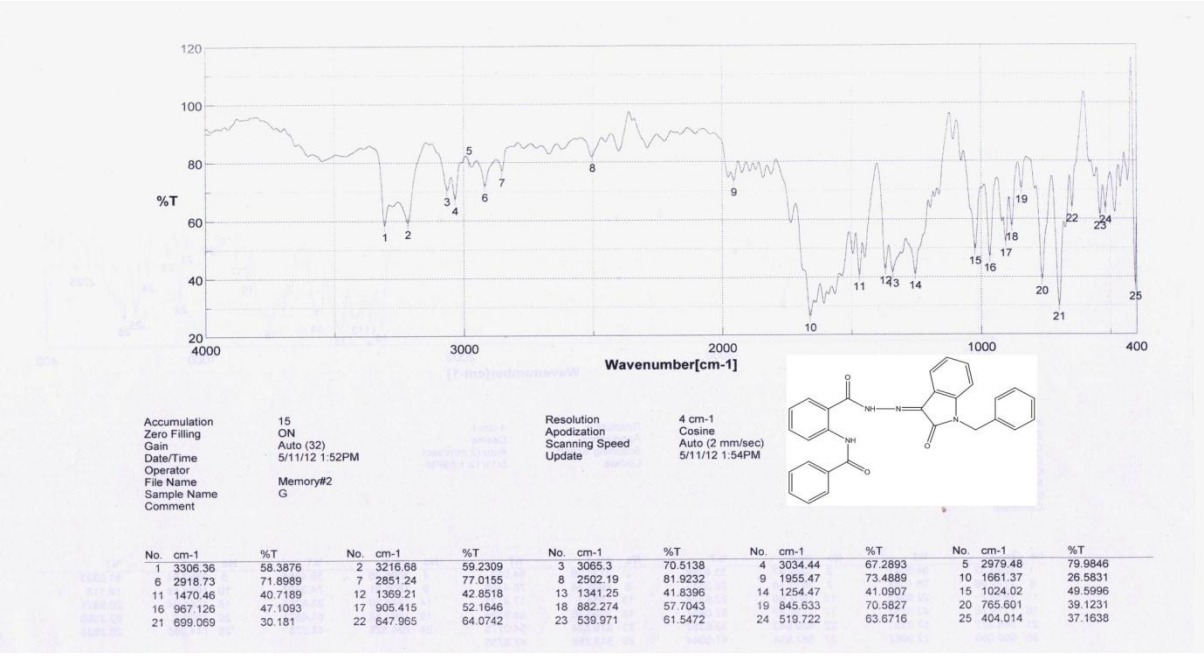


Figure no. 2: FT-IR spectrum of N-(2-(2-(1-benzyl-2-oxoindolin-3-yl) methyl)hydrazine carbonyl) phenyl) benzamide.

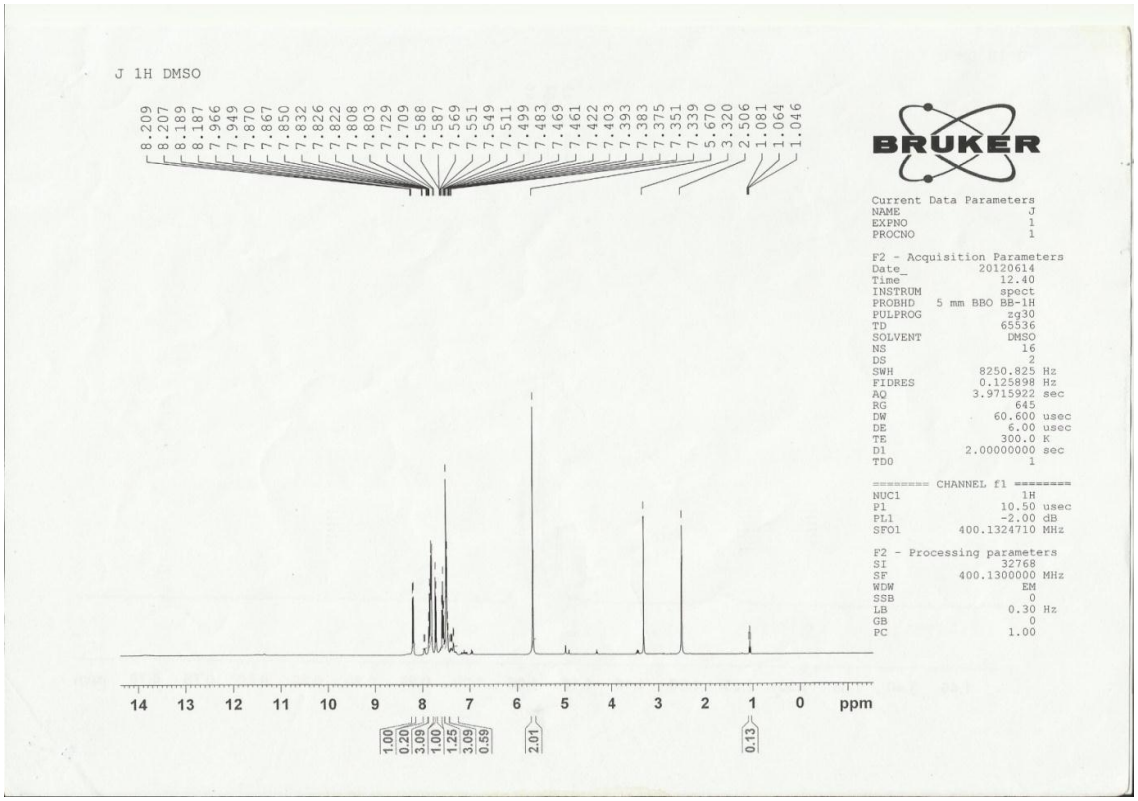


Figure no. 3: ^{1}H-NMR Spectrum of N-(2-(2-(1-benzyl-2-oxoindolin-3-yl) methyl) hydrazine carbonyl) phenyl)benzamide.

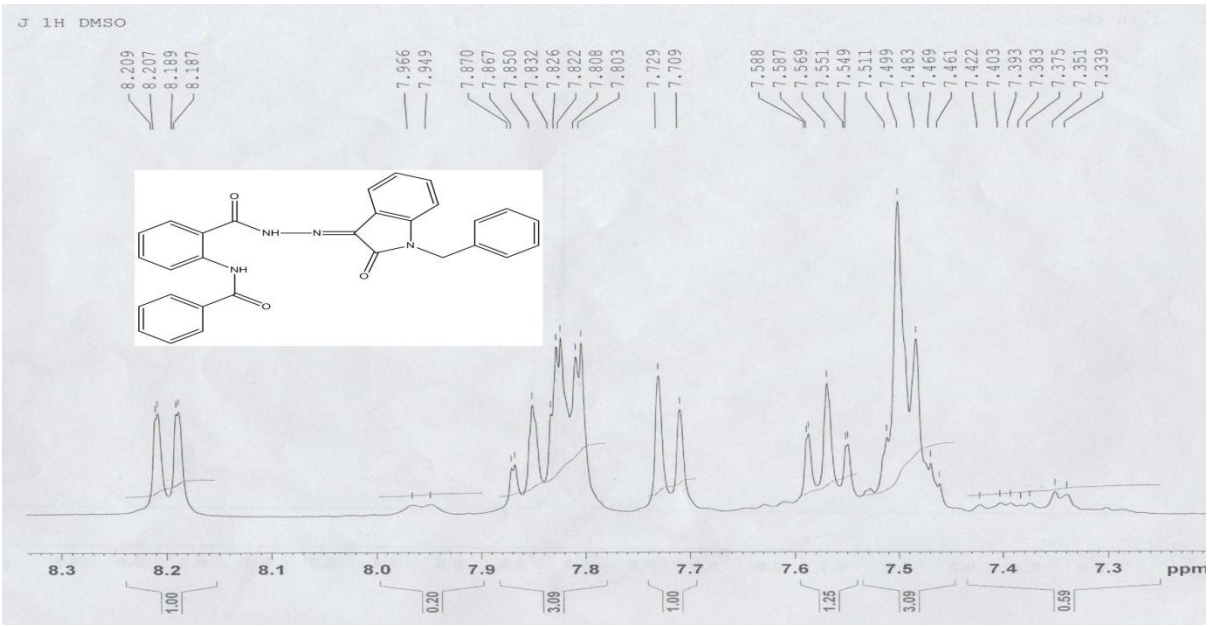


Figure no. 4: Elongated^{1}H-NMR Spectrum of N-(2-(2-(1-benzyl-2-oxoindolin-3-yl) methyl)hydrazine carbonyl)phenyl)benzamide.

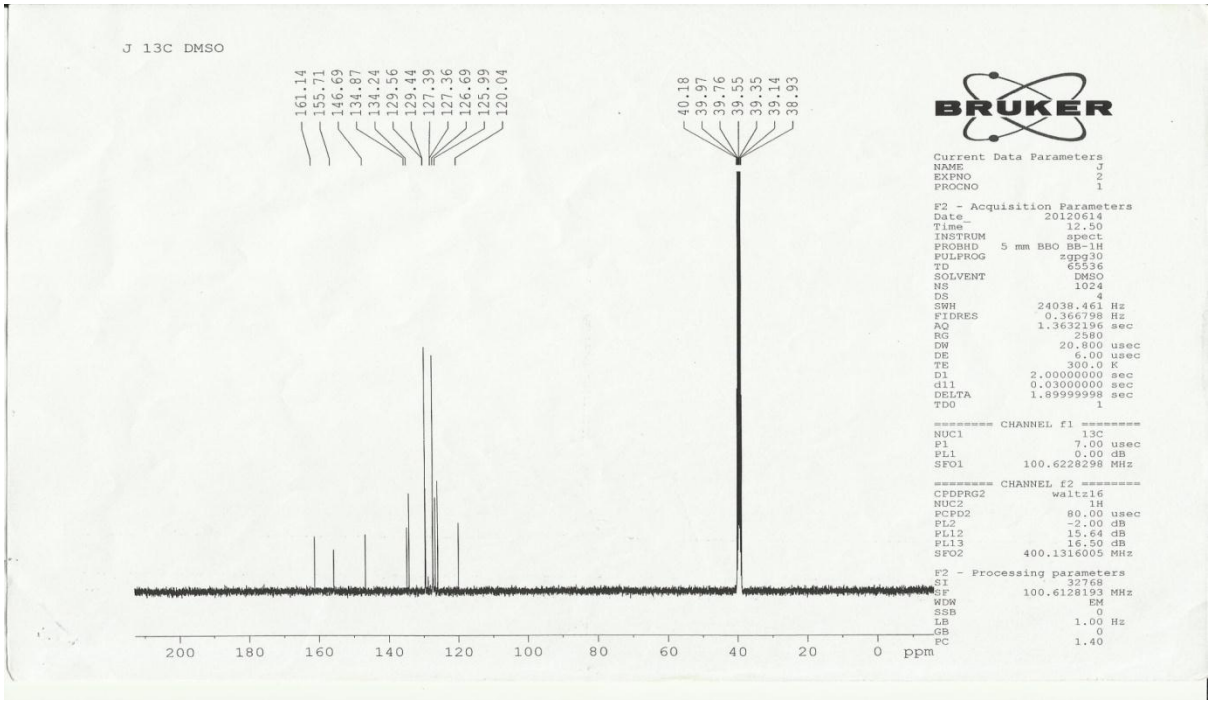


Figure no. 5: ^{13}C-NMR Spectrum of N-(2-(2-(1-benzyl-2-oxoindolin-3-yl) methyl) hydrazine carbonyl) phenyl)benzamide.

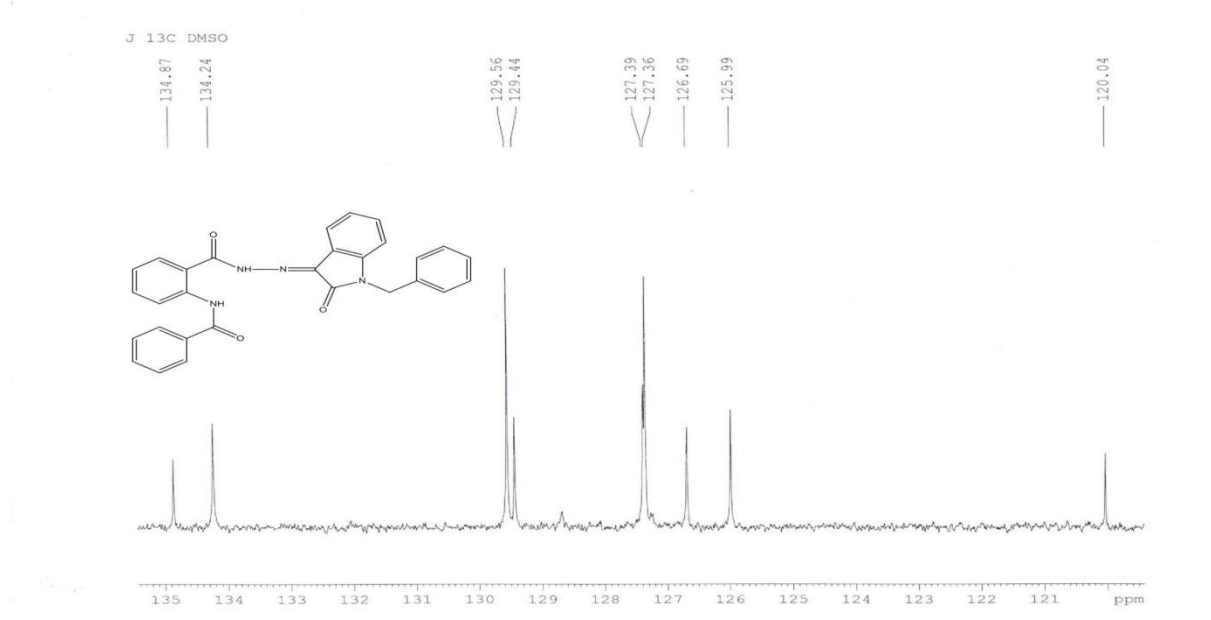


Figure no. 6: Elongated ^{13}C-NMR Spectrum of N-(2-(2-(1-benzyl-2-oxoindolin-3-yl) methyl)hydrazine carbonyl) phenyl) benzamide.

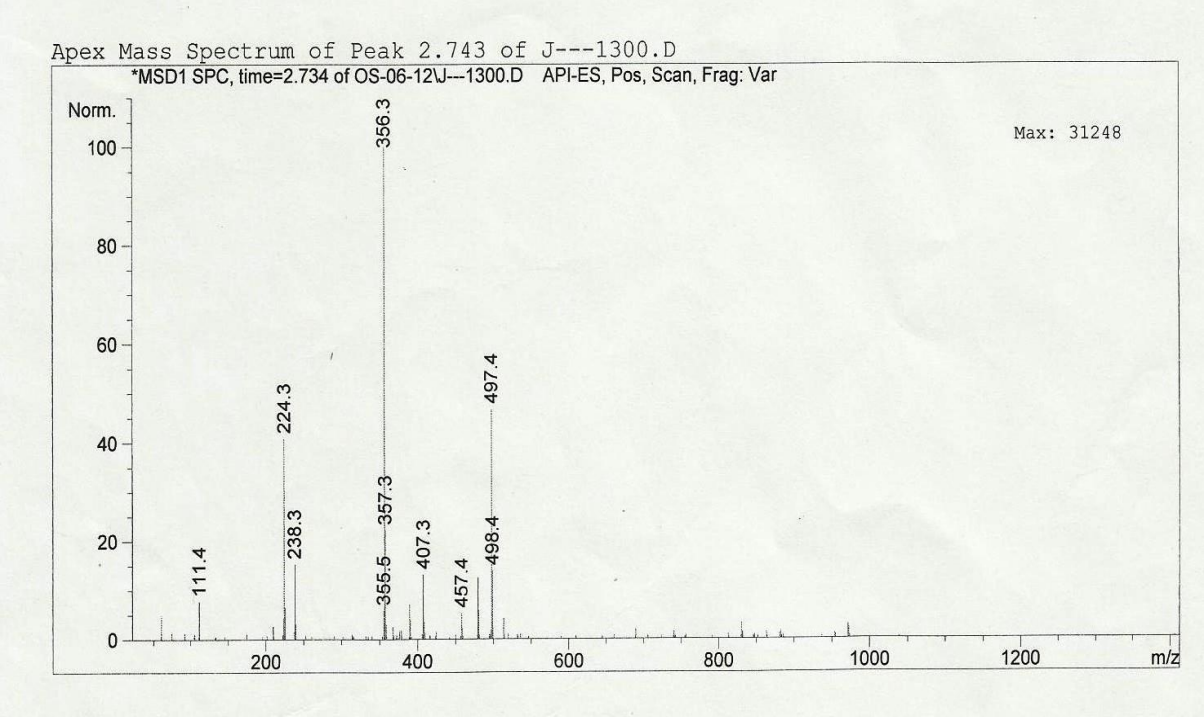


Figure no. 7: Mass spectrum of N-(2-(2-(1-benzyl-2-oxoindolin-3-yl) methyl)hydrazine carbonyl) phenyl) benzamide.

9. SUMMARY AND CONCLUSION

Pharmaceutical chemistry is devoted to the discovery development of new agents for treating diseases. Inorganic compound continue to be important in therapy, for example, as antacids, mineral supplements and radio pharmaceuticals, but organic molecules with increasingly specific pharmacological activities are clearly dominant. The objective of medicinal chemistry is design and production of compounds that can be use as medicine for the prevention, treatment and cure of humans or animal diseases. It is concerned with the invention, discovery, design, identification of biologically active compounds, the study of their metabolism, interpretation of their mode of action at the molecular level and the construction of structure activity relationship (SAR), the relationship between chemical structure and pharmacological activity for a series of compounds. An important aspect of medicinal chemistry has been to establish a relationship between chemical structure and bioological activity. The intellectual goals of researchers are to know the mode of action of drugs at molecular level taken in the prospective sense.

In the present review, interest is focused on the profile of various pharmacological activities of Hydrazones. Hydrazones are a class of Schiff bases which have been found to possess

many biological activities, e.g. antibacterial, anticonvulsant, anti-inflamatory, anti-platelet, anti-depressant, anti-malarial and anti-tubercular, vasodilator effect.

The synthesized compounds were purified by recrystalization from ethanol the purity was checked by M.P and TLC. The synthesized derivatives were characterized with FT-IR, NMR, and Mass spectral data.

1. Chapter I describes about importance, pharmacological activities, chemistry of Hydrazones.
2. Chapter II deals with the literature survey has been discussed with special reference to various Hydrazone derivatives as Analgesic activity, cytotoxic activity, antibacterial and antifungal agents.
3. Chapter III deals with the objective of the entire research work of this dissertation by explaining the need to develop newer derivatives as *invitro* cytotoxic activity.
4. In Chapter IV, a detailed method of synthesis of hydrazone derivatives along with their purification, physical constants have been given. All the compounds were synthesized in good yields and high purity.
5. The compounds were characterized by subjecting to various special studies such as UV, FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectra has been compiled.
6. In Chapter VII deals with the *Invitro* cytotoxic activities of the synthesized hydrazone derivatives and Antimicrobial activity.
7. In Chapter VIII deals with the results and discussion of the hydrazone derivatives Chemistry, Analgesic activity, *Invitro* cytotoxic activity and Antimicrobial activity.
8. In Chapter IX deals with the summary and conclusion of the Synthesized hydrazone derivatives.

CONCLUSIONS

Broadly, the following conclusions could be drawn from the result of these investigations.

1. Synthetic work of these studies could go positively as per the planning and so such in all the reactions carried out, the expected compounds could be obtained.
2. The present work, which has undertaken is bonafied and novel for the synthesis of hydrazone derivatives.
3. In this view I have made an attempt in reviewing the literature on novel hydrazone derivativesfor their medicinal significance with the help of chemical abstract, journals & internet sites.

4. The structures of the hydrazone derivatives were confirmed by UV-Vis, FT-IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectra.
5. The synthesized hydrazone derivatives were screened for their *In vitro* cytotoxic activity and Antimicrobial activity.
6. In vitro evaluation of these hydrazone derivatives revealed cytotoxic activity from 1.2 to > 40µm against CEM, 23 to > 230µm against < L1210, 15 to > 130µm against Molt 4/C8, 12 to >200µm against HL60 & 12 to > 175 µm against BEL 7402.
7. The compound IIIb showing significant cytotoxic activity against all the five cell lines tested in the region of 9, 23, 33, 26, 17µm for CEM , L1210 , Molt 4/C8, HL60 & BEL 7402 respectively. These compounds are compared with standarad drug Melphalan.
8. From the above results it is concluded that the hydrazone derivatives bearing were synthesized and proved inhibitory to tumor growth at submicromolar concentrations. Their compounds however, were not antitumorally active.
9. Significant antibacterial activity was observed for, **IIIc, IIIe** compounds showed significant activity against *K.pneumoniae*. **IIIg** compound showed significant activity against *B.subtilis*, **IIIl** compound showed activity against *E.coli*., **IIIf** compound showed moderate activity against *S.paratyphi, E.coli, B.substilis, K.pneumoniae.*
10. Significant antifungal activity was observed for **IIIa, IIIe** compounds showed significant activity against *Aspergillus nigrum.***IIIb, IIId, IIIl** compounds showed activity against *Aspergillus clavatus*, **IIIc** compound showed significant activity against *Pencilium notatum*, **IIId, IIIg, IIIh** compounds showed significant activity against *Colletotrichem coffeanum.*
11. The synthesized hydrazone derivativespossess surely a better prospectus in future.

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