Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 13s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Design, Characterization And Molecular Docking Of Isatin Derivative

Jadhav Monali D.[1], Jatte Kalleshvar P.[2], Naik Sachin N.[3], Munale Bhagyashri M.[4], Mali Kiran K.[5], Nalawade Rutuja A.[6], Pulate Chetan P.[7]

[1]Department of Pharmaceutical chemistry, Krishna institute of pharmacy, Karad, 415110.

[2]Department of Pharmaceutical chemistry, Dinesh Bembade College of pharmacy, Mahalangra, Latur, 413513.

[3] Department of Pharmaceutics, Dinesh Bembade College of pharmacy, Mahalangra, Latur, 413513.

[4]Department of Pharmacology, Dinesh Bembade College of pharmacy, Mahalangra, Latur, 413513

[5] PhD Research student, Government college of pharmacy, Karad, 415110.

[6]Department of Pharmaceutics, Annasaheb Dange College of Pharmacy, Ashta, Sangali-416301

[7]Department of Pharmaceutical chemistry, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumberwadi, Tal-Junnar, Pune, 410504

***Corresponding Author:**

Jadhav Monali D.[*]

Email ID: mshewale949@gmail.com

Department of Pharmaceutical chemistry, Krishna institute of pharmacy, Karad, 415110.

Cite this paper as: Jadhav Monali D., Jatte Kalleshvar P., Naik Sachin N., Munale Bhagyashri M., Mali Kiran K., Nalawade Rutuja A., Pulate Chetan P., (2025) Design, Characterization And Molecular Docking Of Isatin Derivative. *Journal of Neonatal Surgery*, 14 (13s), 422-431.

ABSTRACT

Isatin (2,3-dioxindole) is an important class of heterocyclic compounds, isatin derivatives are synthetically important substrates, which can be used for many synthesis of a large variety of heterocyclic compounds, and as raw material for drug synthesis. Recently, isatin derivatives have attracted strong interest in organic and medicinal chemistry due to their potent biological and pharmacological activities

Keywords: *Aniline , derivatives , Isatin*

1. INTRODUCTION

Isatin : Isatinis also known as tribulin, is an organic compound derived from indole with chemical formula $C_8H_5NO_2$. The compound was first obtained by Otto Linné Erdman and Auguste Laurent in 1840 as a product from the oxidation of indigo dye by nitric acid and chromic acids [1]. Isatin is a well-known natural product which can be found in plants of the genus Isatis, in Couroupitaguianensis, and also in humans, as a metabolic derivative of adrenaline.It looks in the form of red-orange powder, and it is usually employed as building block for the synthesis of a wide variety of biologically active compounds including antitumorals, antivirals, anti-HIVs, and antituberculars

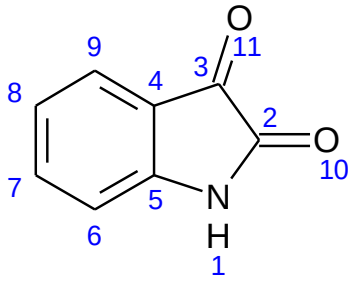


Fig. No. 1 Isatin Structure

Preferred IUPAC Name	1H-Indole-2,3-dione
Chemical Formula	$C_8H_5NO_2$
Molar Mass	147.1308 g/mol
Appearance	Orange - red solid
Melting Point	200 °C

Drug Discovery: Isatin was first discovered by Linne Erdman &Auguste Laurent in the year 1941 from indigo dye. The oxidation of indigo was performed in the presence of nitric acid and chromic acid which resulted in bright orange colored monoclinic crystals of isatin as a product [1].

Significance: The application of heterocycles provides a useful tool for modification of solubility, lipophilicity, polarity, and hydrogen bonding capacity of biologically active agents, which results in the optimization of the ADME/Tox properties of drugs or drug candidates. Isatin (1H-indole-2,3-dione) and its derivatives represent an important class of heterocyclic compounds that can be used as precursors for drug synthesis [2]. Since its discovery, a lot of research work has been done regarding the synthesis, chemical properties, and biological and industrial applications of isatin.

IR Spectroscopy:

- IR its also called as Infrared Spectroscopy.
- IR Spectroscopy is a type of absorption spectroscopy .
- IR is basically used in identification of compound by determining its structure and functional group .
- It is a analytical technique used to determination of qualitative and quantitative analysis of any drug substance by using infrared region of EMR (Electromagnetic Spectrum) [2] .

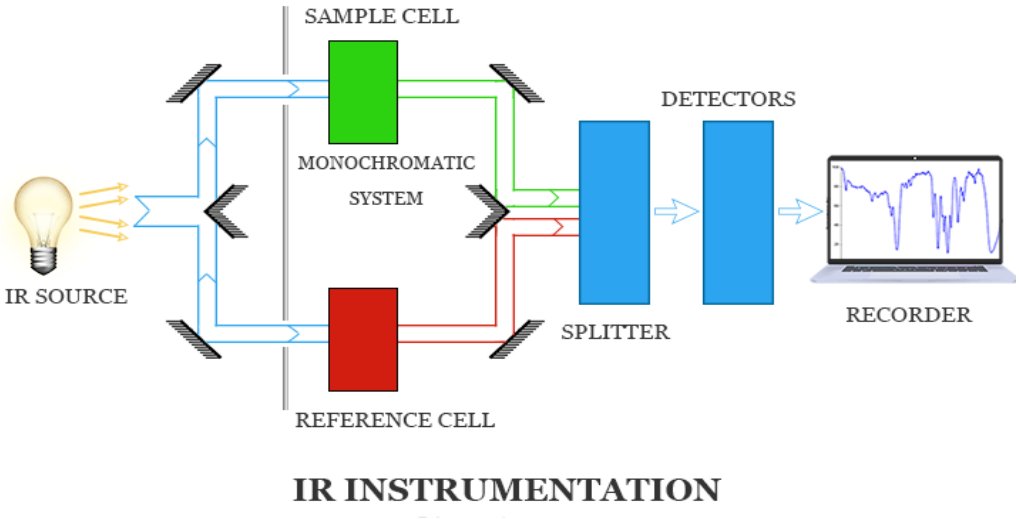


Fig no. 2 IR

Molecular Docking: In the molecular modeling, docking is a method which predicts the preferred orientation of one molecule to a second when a ligand (drug) and a target (receptors) are bound to each other to form a stable complex .The associations between biologically molecules such as proteins, peptides, nucleic acids, carbohydrates, and lipids play a central role in signal transduction. Docking is useful for predicting both the strength and type of signal produced. Molecular docking is most frequently used methods in structure-based drug design, due to its ability to predict the binding-conformation of small molecule ligands to the appropriate target binding site [3]. Characterisation of the binding behaviour plays an important role in rational design of drugs as well as to elucidate fundamental biochemical processes.

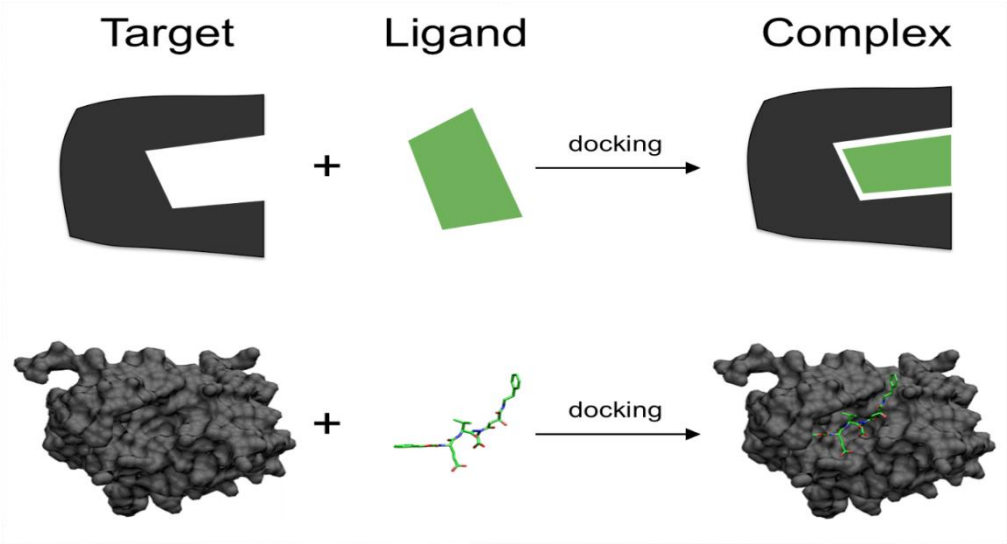


Fig no. 3

2. MATERIALS AND METHODS

Materials :

Table no. 1

Sr.no	**Chemicals**
1)	3-Nitro aniline
2)	Phenylhydrazine
3)	Dichloromethane
4)	Oxalyl Chloride
5)	Aluminium Chloride
6)	Methanol
7)	Ethanol

Methods: Method employed in entire research work framework as well as step by step description of work performed is enlisted below :

- Synthetic scheme is very susceptible to reaction condition all conceivable risk factor are considered and the scheme is optimised from time to time for effective synthetic practices and safest possible outcome

Scheme:

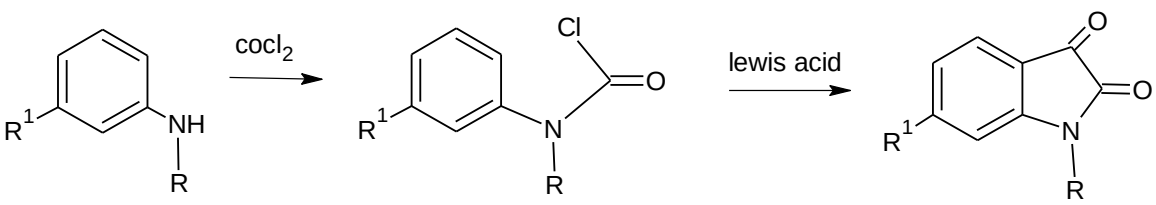


Fig no. 4

Steps involved in the synthesis of derivative synthesis and characterization

Reactant profile :

1] oxalyl chloride :

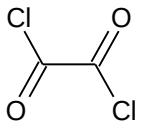


Fig. no.5 Structure

Synonym	Ethanedioyl Choride
molecular formula	$C_2O_2Cl_2$
molecular weight	126.93 g/mol
boiling point	61 °C
Solubility	Ether

a) Scheme 1 - Method with 3-Nitroaniline Derivative :

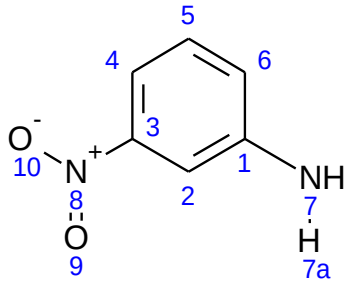


Fig. no. 6 3-Nitroaniline Structure

Chemical Formula	$C_6H_6N_2O_2$
Molar mass	138.126 g/mol^{-1}
Appearance	Yellow solid
Melting point	114^0 C

Reaction :

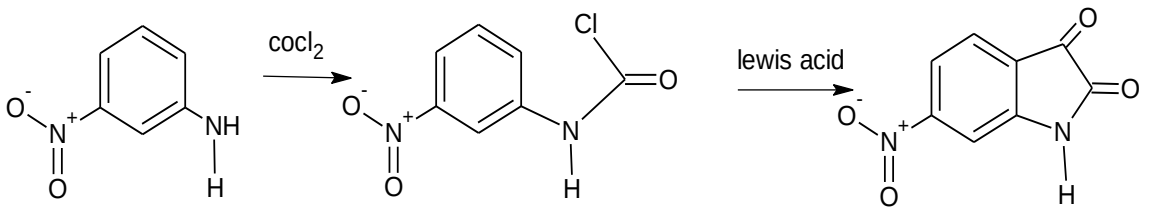


Fig no. 7 Scheme 1 - Synthesis of 6-nitroisatin derivative

R	H
R_1	NO_2

Method for synthesis of Isatin :

Add Solution 0.35 ml of oxalyl chloride in Dichloromethane.

⇩

A solution of 3-nitroaniline derivative (0.5gm) in dichloromethane (3ml) was added dropwise. to cooled (0°c) solution of oxalyl chloride.

⇩

Solution was stirred for 2 hrs in 25 to 30° temp.

⇩

Aluminium Chloride (0.1 gm) added in Methanol (5ml) and refluxed for 7hrs.

⇩

After completion of reaction the product is collected and recrystallized using ethanol(6-nitro-1H-indol-2,3-dione).

Scheme 2 – Method with Phenylhydrazine Derivative :

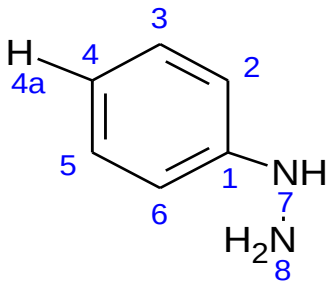


Fig no. 8 Phenylhydrazine structure

Chemical Formula	$C_6H_5NHNH_2$
Molar mass	108.144 g/mol^{-1}
Appearance	Colorless to pale-yellow
Melting point	19.5^0 C

Reaction :

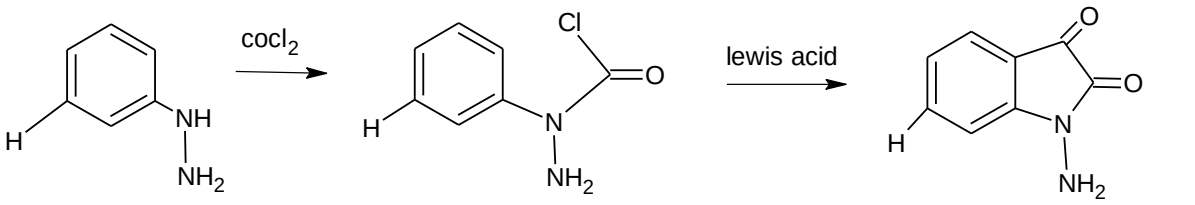


Fig no . 9 Scheme 2-Synthesis of 1-amino-isatin derivatives

R	NH_2
R_1	H

Method for synthesis of Isatin :

Add Solution 0.35 ml of oxalyl chloride in Dichloromethane.

⇩

A solution of Phenylhydrazine derivative (0.5gm) in dichloromethane (3ml) was added dropwise. to cooled (0°c) solution of oxalyl chloride.

⇩

Solution was stirred for 2 hrs in 25 to 30° temp.

⇩

Aluminium Chloride (0.1 gm) added in Methanol (5ml) and refluxed for 7hrs.

⇩

After completion of reaction the product is collected and recrystallized using ethanol.(1-amino1H-indol-2,3-dione)

Synthesized compound are characterized by following methods:

I. Melting Point [11] : The melting point can be determined by introducing a tiny amount of sample into a small capillary tube, attaching this to a thermometer centred in a thiele tube filled with liquid paraffin, heating the tube slowly, and observing the temperatures at which melting begins and is complete.

II. Thin Layer Chromatography: Thin Layer Chromatography can be defined as a method of separation or identification of a mixture of components into individual components by using finely divided adsorbent coated or spread over a chromatographic plate. The mobile phase solvent flows through because of capillary action (against gravitational force). The components move according to their affinities towards the adsorbent. The component with more affinity towards the stationary phase travels slower. The component with lesser affinity towards the stationary phase travels faster [10]. Thus the components are separated on a thin layer chromatographic plate based on the affinity of the components towards the stationary phase.

III. IR : It is a analytical technique used to determination of qualitative and quantitative analysis of any drug substance by using infrared region of EMR (Electromagnetic Spectrum) [2] .

IV. Docking: In the molecular modeling, docking is a method which predicts the preferred orientation of one molecule to a second when a ligand (drug) and a target (receptors) are bound to each other to form a stable complex [3]

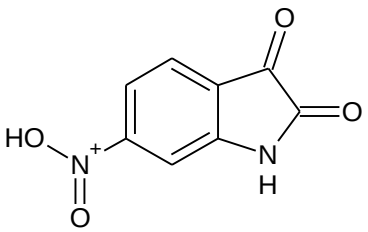
3. RESULTS AND DISCUSSION

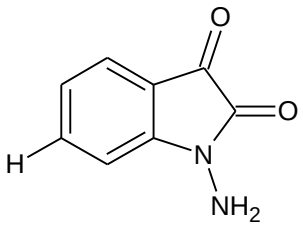
Characterization of derivative :

Table no. 3 Melting point of Aniline derivatives

Compound no.	R group added	R1 group added	melting point
A)	H	NO_2	114 ° C
B)	NH_2	H	19.5 ° C

Table no. 4 Structure and IUPAC name of synthesized derivative

Compound no.	structure	IUPAC
A)		6-Nitro-1H-indol-2,3-dione

B)		1-amino-1H-indol-2,3-dione

FT-IR Results:

IR Spectrum of 3-Nitro Aniline derivative :

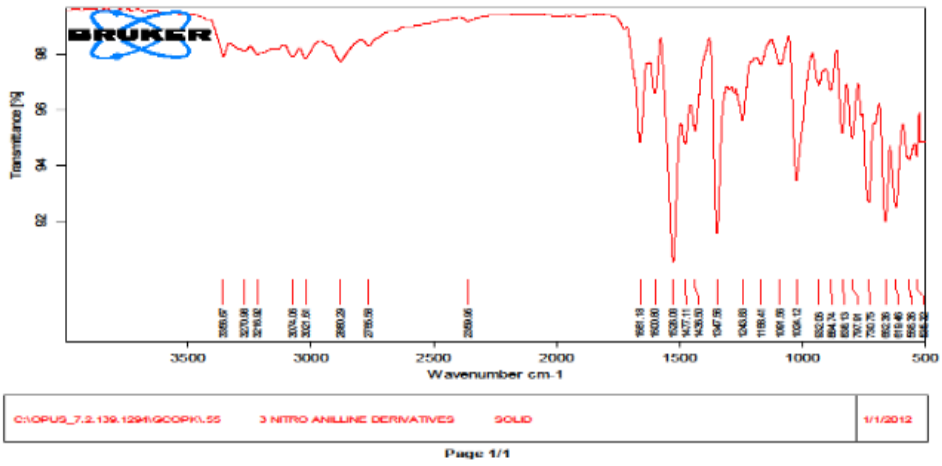


Fig no. 10

Table no . 6

Functional Group	**Standard Frequencies (cm^{-1})**	**Observed Frequencies (cm^{-1})**
N-H	3400-3000	3213.26
C-O-C	700-800	758.82
Aromatic C-HStreching	3100-3000	3035.38
N-O	1550-1365	1477.11

IR Spectra shows the presence of the specific functional group at specific frequencies.

IR Spectrum of Phenylhydrazine derivative :

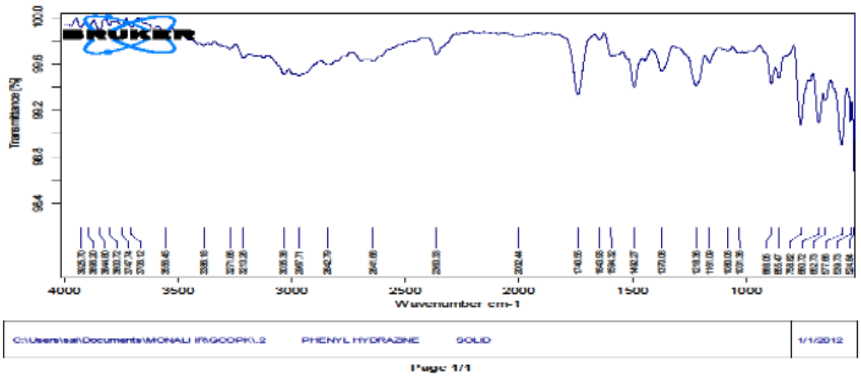


Fig no. 11

Table no . 7

Functional Group	**Standard Frequencies (cm^{-1})**	**Observed Frequencies (cm^{-1})**
C-C	1172-1157	1168.41
N-H	3400-3000	3216.92
C-H	2960-2850	2880.29
C-O-C	700-800	730.75
Aromatic C-H Streching	3100-3000	3021.61

- IR Spectra shows the presence of the specific functional group at specific frequencies .

Derivative profile

Compound A : 6-Nitro-isatin

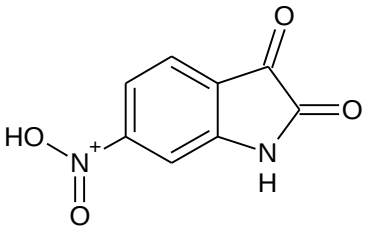


Fig no. 12 structure

IUPAC Name :6-nitro-1H-indol-2,3-dione

Properties:

- Colour: Cream colour
- Melting Point: 123°C
- Molecular Formula: $C_8H_4N_2O_4$
- Theoretical Yield: 1.39gm
- Percentage Yield: 49.64%
- Practical Yield: 0.69mg

Compound B : 1-amino-isatin

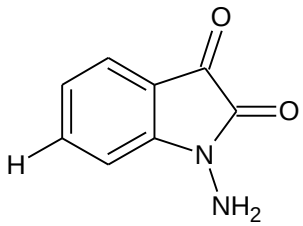


Fig no. 13 structure

IUPAC Name : 1-amino-1H-indol-2,3-dione

Properties:

1. Colour: Pale-yellow
2. Melting Point: 25°C
3. Molecular Formula: $C_8H_6N_2O_2$
4. Theoretical Yield: 1.5gm
5. Percentage Yield: 48%
6. Practical Yield: 0.72 mg

Molecular Docking Result : Isatin derivatives are reported to show anti-tubercular activities, accordingly, isatin is a versatile lead molecule for designing of potential anti-tubercular agent. Some of these derivatives are natural products, for example, tryptanthrin, an alkaloid from the Chinese herb Stro-bilanthescusia showed potent activity against MTB H37Rv (1mg/l) .

Table no. 8

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
4rye_ligand	-4.8	0	0
4rye_ligand	-4.6	5.784	4.292
4rye_ligand	-4.5	9.059	6.425
4rye_ligand	-4.4	8.401	6.239
4rye_ligand	-4.4	6.045	3.752
4rye_ligand	-4.3	2.635	1.847
4rye_ligand	-4.3	4.642	3.243
4rye_ligand	-4.2	6.542	4.324
4rye_ligand	-4.2	3.142	1.938

4. CONCLUSION

The isatin scaffold can be found in a broad range of natural and synthetic compounds of medicinal im-portance. Isatin is a versatile lead molecule for potential bioactive agents and its derivatives were reported to possess potent pharmacology . In the mean time no isatin derivative clinically used in different therapy, however, research will hopefully continue to shed light on ways to increase the therapeutic efficacy and specificity of isatin derivatives.

REFERENCES

[1] AJMER SINGH GREWAL∗ JCDM College of Pharmacy, Sirsa-125055, Haryana (India)

[2] Da Silva JFM, Garden SJ, Pinto AC, The chemistry of isatins: a review from 1975 to 1999, Journal of Brazilian Chemical Society, 2001; 12(3): 273-324.

[3] Bhrigu B, Pathak D, Siddiqui N, Alam MS, Ahsan W, Search for biological active isatins: a short review, International Journal of Pharmaceutical Sciences and Drug Research, 2010; 2(4): 229-235.

[4] Chen et al. Chemistry Central Journal 2011

[5] Vendemiale G, Grattagliano I, Altomare E: An update on the role of free radicals and antioxidant defense in human disease. Int J Clin Lab Res 1999, 29:49-55.

[6] Valko M, Rhodes CJ, Moncol J, Izakovic M, Mazur M: Free radicals, metals and antioxidants in oxidative stress-induced cancer. Chem Biol Interact 2006, 160:1-40.

[7] Cooke MS, Evans MD, Dizdaroglu M, Lunec J: Oxidative DNA damage: mechanisms, mutation and disease. FASEB J 2003, 17:1195-1214.

[8] Journal of Advanced Pharmaceutical Technology & Research | Jul-Sep 2010 | Vol 1 | Issue 3

[9] Article *in* International Journal of Research in Pharmaceutical Sciences · April 2010

[10] Aboul-Fadl T, Mohammed FA, Hassan EA. Synthesis, Antitubercular Activity and Pharmacokinetic Studies of

Some Schiff Bases Derived from 1- Alkylisatin and Isonicotinic Acid Hydrazide (INH). Arch. Pharm. Res. 2003, 26: 778–784.

[11] Bal TR, Anand B, Yogeeswari P, Sriram D. Synthesis and evaluation of anti-HIV activity of isatin β-thiosemicarbazone derivatives. Bioorg. Med. Chem. Lett. 2005, 15: 4451– 4455.

[12] Ballell L, Field RA, Duncan K, Young RJ. New small-molecule synthetic antimycobacterials. Antimicrob. Agents Chemother. 2005, 49: 2153–2163.

[13] Medvedev A, Buneeva O, Gnedenko O, Ershov P, Ivanov A, et al. (2018) Isatin, an endogenous nonpeptide biofactor: A review of its molecular targets, mechanisms of actions, and their biomedical implications. Biofactors 44(2): 95-108