Isatin is an endogenous compound identified in humans that possesses a wide range of biological activities. Isatin has anxiogenic, sedative, anticonvulsant activities and acts as a potent antagonist on atrial natriuretic peptide receptors in vitro. A series of p-substituted isatin semicarbazones have shown anticonvulsant activity in MES, scPTZ and scSTY tests. Various isatin-N-Mannich bases of isatin-3-thiosemicarbazones have shown antiviral and tuberculostatic activity. Methisazone is an effective compound against variola and vaccinia viruses. The N-dimethyl and morpholino derivative of 5-methyl isatin and trimethoprim exhibited an EC$_{50}$ of more than 4.3 and 17.7 μg mL$^{-1}$, respectively. Isatin (3-o-nitrophenyl) hydrazone has shown activity against Walker carcinoma-256. Various substituted indolinones showed antitubercular activity against M. tuberculosis H$_{37}$Rv with MIC ranging from 10–20 μg mL$^{-1}$. Isatin derivatives of Mannich bases had fibrinolytic, muscle relaxant, antiallergic, immunosuppressant, and antithrombotic activity. Isatin showed cardioinhibitory effect on frog heart, and hypotensive, respiratory depression and antidiuretic effects.

Keywords: isatin, Mannich bases, semicarbazones, anticonvulsant, antimicrobial, antitubercular effects

Isatin (2,3-dioxindole) is an endogenous compound identified in humans, and its effect has been studied in a variety of systems. Biological properties of isatin include a range of actions in the brain and offer protection against certain types of infections.

CNS ACTIVITIES

CNS depressant activities. – Isatin has a range of actions such as CNS-MAO inhibition, anticonvulsant and anxiogenic activities. Its effect as a mono amino-oxidase (MAO) inhibitor is the most potent in vitro action recorded to date. It is a selective MAO B inhi-
bitor with an inhibitory concentration \( (I_{C_{50}}) \) of about 3 \( \mu \)g mL\(^{-1} \) (1). At higher concentrations it inhibits a variety of other enzymes, such as alkaline phosphatases. In rodents, it has been reported to act as an antiseizure agent and to potentiate the antiseizure action of propranolol. Isatin has also been found to increase vigilence (2). At a low dose (15 mg kg\(^{-1} \)), it is anxiogenic and prolongs pentylenetetrazole (PTZ) induced seizures while at higher dosage (80 mg kg\(^{-1} \)) it becomes sedative and anticonvulsant and the brain 5-HT levels are found to be significantly raised (3).

**Anticonvulsant activity.** – Bhattacharya and Chakraborti (4) reported isatin to be an endogenous compound with anxiogenic properties, which occur within a narrow intraperitoneal (i.p.) dose range (15–20 mg kg\(^{-1} \)). Higher doses exhibited a significant anticonvulsant effect against both PTZ and 3 MPA (mercapto propionic acid) induced clonic convulsions. Bhattacharya et al. (5) have found isatin to function as a potent antagonist on anti-natriuretic peptide (ANP) receptors \textit{in vitro}, and to inhibit anxiolytic, memory facilitating and diuretic actions of intracerebroventricularly administered ANP.

Li et al. (6) studied the inhibitory effect of isatin on amygdaloid kindling in rats, seizure and anticonvulsant effect in convulsion models. Isatin (50–200 mg kg\(^{-1} \)) given i.p. significantly raised the focal after-discharge threshold (ADT), reduced the seizure severity and percentage of generalized seizure \((p < 0.01)\) in kindled rats.

Pajouhesh et al. (7) synthesized a series of cyclohexane and other cyclic ketone derivatives of isatin and screened them for anticonvulsant activity (Fig. 1). A considerable number of analogues were active in pentylenetetrazole seizure threshold tests. However, no consistent structure to activity pattern was recorded.

Jain and Bansal (8) synthesized a series of condensed compounds by reacting a heterocyclic system like isatin/5-fluoroisatin with ethyl cyano acetate and substituted ketones. The structure represented in Fig. 2 showed anticonvulsant activity in rats.

Blackburn et al. (9) reported that indoles, such as 1-\{5-(2-thienyl methoxy-1H-indol-3-yl) propan-2-amine, were used in the treatment and prevention of epilepsy and migraine.
Difabio et al. (10) synthesized substituted indole-2-carboxylates as in vivo potent antagonists acting at the strychnine insensitive glycine binding site and evaluated their in vitro potency to inhibit convulsions induced by N-methyl-D-aspartate (NMDA) in mice.

Olesen and Kanstrup (11) prepared pyrido[2,3-b]indoles to treat a disease in the CNS via the metabotrophic glutamate receptor system. The title compounds are useful for treating diseases in the CNS such as epilepsy, senile dementia and Parkinsonism (Fig. 3).

Sharaf (12) investigated pyrroloindoles and indolethiazepines for their anticonvulsant, analgesic, anti-inflammatory and ulcerogenic activities. All the compounds showed potent anticonvulsant and analgesic activities.

Evanno et al. (13) synthesized 1H-pyrido[3,4-b]indole-4-carboxamide derivatives of the structure presented in Fig. 4.

The different substituted compounds (Fig. 4) were tested for their anxiolytic, hypnotic and anticonvulsant activities.

Jakobsen et al. (14) prepared thieno[2,3-b]indoles and pyrido[2,3-b]indoles as antagonists on the metabotropic glutamate receptor and therefore useful in treating CNS diseases such as epilepsy, Parkinsonism and senile dementia (Fig. 5).
Evanno et al. (15) synthesized 4-oxo-3,5-dihydro-4-\(H\)-pyridazano-4,5-b-indole-1-acetamide derivatives that can be used for treating diseases related to GABA aminergic (GABA – gamma amino butyric acid) transmission disorders. The compounds also showed hypnotic and anticonvulsant activities in rats and mice. The structures of the compounds are given in Fig. 6.

Karali et al. (16, 17) synthesized a series of 3-thiosemicarbazono-2-indolinones (Fig. 7). Hydrazides (\(R = \text{Br, Cl} \); \(R^1 = \text{OC}_2\text{H}_5, \text{N}_2\text{H}_3\)) were prepared from the appropriate furyl dihydro triazolethiones. Subsequent treatment of 2-furoic hydrazide-2,3-indoline- or 3-bromo-2,3-indolinedione furnished the corresponding 3-hydrazono-2(1H)indolinones. Two of the new compounds showed anticonvulsant activity in preliminary tests.
Reddy et al. (18) prepared indolinyl and tetrahydro quinolyl carboxamidines. \(N\)-(1-naphthyl)-1-indolinyl carboxamidine at 2 mg kg\(^{-1}\) i.p. caused 82% inhibition of seizures in mice.

Gursoy and Karali (19) synthesized a new series of 3-aryloxyl, arylthioxy acetyl hydrazono-2-indolinones (Fig. 8) and 1-morpholino methyl-3-aryloxyl-aryl thioxy acetyl hydrazono-2-indolinones.

Anticonvulsant evaluation of these compounds revealed varying degrees of activity against pentylenetetrazole induced seizures.

Popp and Donigan (20) synthesized three series of compounds, namely, 3-hydroxy-3-phenacyloxindoles (Fig. 9).

3-Phenacyclidine-2-indolinone was active at both 100 and 300 mg kg\(^{-1}\) in the maximal electroshock seizure test.

Galambos (21) prepared racemic or optically active 3-spiroxindole derivatives (Fig. 10).
The isatylidene derivative in Fig. 10. has antihypoxic activity, anticonvulsant activity and provides protection from pentyleneetetrazole induced brain oedema.

Ghaney and El-Helby (22) synthesized new 1,3-dioxo-N-phenyl-2H-isoindole-2-acetamides (Fig. 11) by condensation of chloroacetanilides with the potassium salt of 1H-isoindole-1,3-dione in DMF.

Preliminary pharmacological screening of some of the new compounds showed that they could have marked anticonvulsant activity against pentyleneetetrazole-induced convulsions in frogs.

David et al. (23) have shown that 2-aminonapthyridine is prepared by ring cleavage of 2-isoindolinyl napthyridine (Fig. 12).

These compounds have exhibited remarkable anxiolytic, hypnotic, anticonvulsant and muscle relaxant properties.

Smith et al. (24) investigated the role of nitric oxide in epilepsy. The neuronal selective nitric oxide synthase inhibitor, 7-nitroindazole (7-NI), is an anticonvulsant. The effect of 7-NI in rodents with reflex epilepsy may result from arginine accumulation or a reduction of nitric oxide or L-citrulline formation. Alabadi et al. (25) reported that 7-nitroindazole increases hippocampal extracellular glutamate concentration in status epilepticus induced by kainic acid in rats.

Srivastava et al. (26) synthesized a series of compounds from carbazole, which on condensation with chloroacetyl chloride in the presence of triethylamine afforded aze-
Azetidinones. Some of the compounds exhibited promising antibacterial, antifungal, anti-inflammatory and anticonvulsant activities (Fig. 13).

Singh et al. (27) synthesized a series of isatin-based spiroazetidinones and screened them for their anticonvulsant activity (Fig. 14).

Pandeya et al. (28) synthesized a series of p-nitrophenyl substituted semicarbazones and their anticonvulsant activity was screened against maximal electroshock (MES), subcutaneous pentylenetetrazole (scPTZ) and subcutaneous strychnine (scSTY) tests (Fig. 15).

All the compounds were active in scPTZ and MES tests. Two compounds were active in the MES test at 100 mg kg⁻¹.

Pandeya et al. (29) synthesized a series of N-methyl/acetyl-5-(un)substituted-isatin-3-semicarbazones (Fig. 15).

In this series, compounds with 4-bromo and 2-chloro substitution (R = 4-Br and 2-Cl) showed promising activity and were also active in MES, scPTZ and scSTY induced tests.

Further, Pandeya et al. (30) synthesized halosubstituted isatin semicarbazones to study the role of hydrogen bonding for anticonvulsant activity (Fig. 16).

Pandeya et al. (31) synthesized a series of p-nitrophenyl substituted semicarbazones and phenoxy/p-bromophenoxy acetyl hydrazones and their anticonvulsant activity was screened against MES, ScPtz and ScSty (Fig. 17). Compounds with NHCO- group were found to be the most active in all these tests. These compounds were also active in the MES test after oral administration in rats. On the other hand, compounds with -OCH₂ group were devoid of anticonvulsant activity. The studies revealed that the hydrogen-bonding domain in semicarbazones, adjacent to the lipophilic aryl ring, is essential for the anticonvulsant activity.
Pandeya et al. (32) had synthesized Schiff bases of N-methyl and N-acetyl isatin derivatives with different aryl amines and screened them for anticonvulsant activity against MES and scMet. N-methyl-5-bromo-3-(p-chlorophenylimino) isatin exhibited anticonvulsant activity in MES and scMet with $LD_{50} > 600$ mg kg$^{-1}$, showing better activity than the standard drugs such as phenytoin, carbamazepine and valproic acid (Fig. 18).

Anxiogenic and other CNS activities. – Palit et al. (33) studied the behavioral effects of isatin, a putative biological factor in rhesus monkeys. Isatin, one of the constituents of tribulin, a postulated endocoid marker of stress and anxiety, has been shown to induce
anxiety in rodents. Medvedev et al. (34) studied a range of isatin analogues for their *in vitro* inhibition of human MAO A and B. Most analogues were less potent than isatin. Hydroxylation of the aromatic ring in isatin changed the inhibitory potency in favour of MAO A, with 5-hydroxy isatin being a potent and selective MAO A inhibitor (IC$_{50}$ 8 µg mL$^{-1}$). Isatinic acid, which is formed reversibly from isatin in alkaline medium, showed no inhibition (Fig. 19).

The QSAR (Quantitative Structure Activity Relationship) analysis revealed the requirement of co-planar structure of substituents at C$_2$ and C$_3$ for selective MAO A inhibition. Hamaue et al. (35) have shown that isatin is an endogenous inhibitor of MAO and that it has several physiological properties for stress and anxiety following extensive experimental and clinical investigations. Isatin has an inhibitory effect on acetylcholine esterase (AchE). This study elucidated the effect of isatin administered exogenously on the acetylcholine and dopamine (DA) levels of brain tissues in rats. These results suggest that endogenous isatin may play a role in regulating the brain levels of acetylcholine by increasing the level of dopamine. Stress conditions, like acute food deprivation and acute cold exposure, were found to markedly increase the urinary excretion of isatin, as reported by Tozawa and Veki (36).

Sarangapani and Reddy (37) synthesized isatin N-(2-alkyl-benzoxazole-5-carbonyl) hydrazones and screened them for analgesic, antidepressent and H$_1$-antihistaminic activities.

Kennis et al. (38) synthesized hexahydropyrido (4,3-b) indole derivatives.
The compound displayed in Fig. 20. was found to have central dopamine and serotonin antagonistic activity in the combined apomorphine, tryptamine and nor-epinephrine test in rats.

CHEMOTHERAPEUTIC ACTIVITIES

Antimicrobial activity. – Varma and Nobles (39) investigated various isatin-N-Mannich bases of isatin-3-thiosemicarbazone derivatives against viral, fungal and bacterial organisms (Fig. 21). Thioureas of different carbonyl compounds have shown antiviral and tuberculostatic activity. Three compounds from this series were toxic to cancer cells and two compounds were active against Polio virus type II, against Gram positive bacteria, fungi and yeast. The same authors (39) synthesized isatin N-Mannich bases of the structure shown in Fig. 21.

![](Fig. 21. Isatin-3-thiosemicarbazone derivatives.)

Nine compounds showed activity against Polio II virus, one compound displayed activity against four different viruses, two compounds (R = H, R1 = p-propylbenzyl-piperidino; R = Br, R1 = morpholino) showed activity against all four types of organisms (Gram positive bacteria, Gram negative bacteria, acid fast bacteria, yeast and fungi).

Kupinić et al. (40) synthesized a congenic series of isatin N-Mannich bases and evaluated their antimicrobial activities (Fig. 23).

![](Fig. 22. Isatin N-Mannich bases.)

![](Fig. 23. Isatin N-Mannich bases.)
Most of the above-synthesized compounds strongly inhibited Gram-negative bacteria and fungi but only moderately inhibited the growth of Gram-positive bacteria. Three compounds (R₁ = H, R₂ = NNHCOCH₃, R₃ = H; R₁ = C₂H-C₄H₈NO, R₂ = NNHCSNH₂, R₃ = H; R₁ = H, R₂ = NNHCOOH, R₃ = H) were most active against the Gram-positive bacterium Micrococcus flavus.

A series of 5-haloisatins were amino methylated in position 1 and hydrazino groups were introduced in position 3 by Maysinger et al. (41). The synthesised N-Mannich bases and hydrazones were tested against various bacteria and fungi. Halogen in position 5 and an amino moiety in position 1 showed better activity than unsubstituted isatin. The most biologically active compound was found to be the di-i-propyl amino N-Mannich base of 5-chloroisatin.

Daisley and Shah (42) investigated the antimicrobial and antifungal activities of a series of 5-nitro-3-phenyl iminoindol-2-(3H)-ones and their 1-piperidino methyl analogues (N-Mannich bases). Growth inhibition of Gram positive bacteria was observed with little or no activity against Gram negative bacteria. Antifungal activity was absent.

Dilber et al. (43) synthesized many isatin and N-alkylisatin derivatives by the Reformatsky reaction (Fig. 24). The synthesized compounds were screened against Escherichia coli, Staphylococcus aureus and Saccharomyces cerevisiae. Two compounds were found to be active against S. aureus and E. coli.

Pandeya and Sriram (44) synthesized Schiff bases of isatin and its derivatives with trimethoprim and their N-Mannich bases (Fig. 25). All the synthesized compounds showed good activity against Vibrio cholerae, Shigella boydii, Enterobacter faecalis and Edwardsiella tarda with MIC (Minimum Inhibitory Concentration) in the range of 10–25 μg mL⁻¹. Some compounds were found to be active against Salmonella typhi and Vibrio cholerae 0139; two compounds inhibited HIV-1 (IIIIB) with EC₅₀ of 7.6 and 12.3 μg mL⁻¹.

Pandeya et al. (45) synthesized Schiff bases of isatin and 5-methyl isatin with sulfadoxine (Fig. 25). All the compounds showed notable activity when compared to sulphadoxine. The piperidino methyl compounds were found to be the most active ones in the series. Six compounds were active against Candida albicans, Candida neoformis, Histoplasma capsulatum, Microsporum audounii and Trichophyton mentagrophytes at a concentration of 100 μg mL⁻¹. The compound containing piperidino methyl group showed appreciable activity (10%) against the HIV-2 (ROD) strain.

Mannich bases of ciprofloxacin and lomefloxacin were synthesized by Pandeya et al. (46). Isatin Mannich bases of ciprofloxacin were equivalent or more potent than ciprofloxacin against E. coli, V. cholerae, Staphylococcus epidermidis, Klebsiella pneumoniae and
Pseudomonos aeruginosa. Mannich bases of lomefloxacin were equipotent to those of lomefloxacin (Fig. 26).

Pandeya et al. (47) reported the synthesis of $N$-[(4' chloro phenyl) thiazol-2-yl] thiosemicarbazide and its 5-chloro and 5-bromo derivatives. $N$-Mannich bases of these compounds were also synthesized. Antimicrobial activity of compounds was tested against 28 pathogenic bacteria and 8 pathogenic fungi, and anti-HIV activity against HIV-1 (IIIB) in MT-4 cells. 1-$N,N$-dimethylaminomethyl-5-bromoisatin-3-$1'$-$4''$-[(p-chlorophenyl)thiazol-2''-yl]thiosemicarbazone showed the most favourable activity. The same group (48) reported the synthesis of $N$-(6-chlorobenzthiazol-2-yl) thiosemicarbazide and its $N$-Mannich bases. Antimicrobial activity of the above compound against 25 pathogenic bacteria was investigated. Results indicated that $1-[N,N$-dimethylaminomethyl] isatin-3-$1'$-$6'$-chlorobenzothiazol-2'-yl] thiosemicarbazone was the most active among the synthesized compounds.

Synthesis, antimicrobial and anti-HIV evaluation of 3-amino-2-methyl mercapto quinazolin-4-(3H)-one Schiff bases of 5-chloro, 5-bromo isatins and their $N$-Mannich bases
were reported by Pandeya et al. (49). 5-Chloro-3-(3’,4’-dihydro-2’-methyl-mercapto-4-oxo-quinazolin-3’-yl)-1-morpholino methyl imino isatin was reported to be the most active antimicrobial agent among the compounds synthesized. None of them showed appreciable anti-HIV activity.

Pandeya et al. (50) investigated antimicrobial and anti-HIV activity of 3-(4’-pyridyl)-4-amino-5-mercapto-4-(H)-1,2,4-triazole Schiff base and N-Mannich bases of isatin. Among the synthesized compounds, 1-(piperidino methyl)-3-bromo-[3’-(4’-pyridyl)-5’-mercapto-4’(H)-1’2,4’-triazol-4’-yl] imino isatin showed the most favourable antimicrobial activity. None of them showed appreciable anti-HIV activity.

Methisazone (N-methyl isatin-3-thiosemicarbazone) (Fig. 27) was found to be an effective compound against variola and vaccinia viruses (51).

![Fig. 27. Methisazone (N-methyl isatin-3-thiosemicarbazone).](image)

As given by Teitz et al. (52), N-methyl isatin-β-4’,4’-diethylthiosemicarbazone and N-allyl-β-4’,4’-diallyl thiosemicarbazone (Fig. 28) have shown inhibition of HIV by their action on reverse transcriptase and viral structural proteins.

![Fig. 28. Isatin thiosemicarbazone derivatives.](image)

Webber et al. (53) reported the design, synthesis and biological evaluation of reversible, non-peptidic inhibitors of human rhinovirus (HRV) 3C protease (3CP). A novel series of isatins were designed (Fig. 29).

![Fig. 29. Isatine derivatives – reversible inhibitors of rhinovirus 3CP.](image)
All the compounds were tested for inhibition of purified HRV-14 3CP. Three compounds 
(R = CONH₂, R¹ = CH₃ or CH₂ = CHC₆H₅ or CH₂(4-CH₃-C₆H₄) were found to have ex-
cellent selectivity for HRV-14 3CP compared to other proteolytic enzymes, including 
chymotrypsin and cathepsin B.

Britcher and Susan (54) synthesized 3-substituted heterocyclic inhibitors of HIV re-
verse transcriptase (Fig. 30).

Optionally, oxidized at N and S and/or substituted, those indols and their pharma-
ceutically acceptable salts are useful as inhibitors of HIV reverse transcriptase, preven-
tion or treatment of HIV infection.

HIV protease inhibitors were disclosed by Vacca et al. (55) (Fig. 31).

Artico et al. (56) prepared 1H-pyrrol-1-yl and 1H-indol-1-yl aryl sulfones for treat-
ment of HIV-1 infections.
Anticancer activity. – Popp and Pajouhesh (57) synthesized 3-o-nitrophenyl hydrazones of isatin by condensation of isatin with o-nitrophenyl hydrazine (Fig. 32). These compounds were found to be active intramuscularly against Walker carcinoma-256 and inactive against L-1210 lymphoid leukaemia.

A novel series of 5-(2-oxo-3-indolinyl) thiazolidine-2,4-dione having positions 1 and 3 of the isatin and thiazolidine rings, respectively, substituted by various Mannich bases were prepared by Eshba and Salama (58) (Fig. 33).

Five compounds were evaluated for antileukaemic activity against p388 lymphocytic leukaemia in the mice. The di-Mannich base with a dimethyl amino component exhibited the highest activity of the tested compounds. Introduction of bromine into the aromatic moiety of the isatin ring at position 5 increased the activity among the parent molecule to a smaller extent.

Teitz et al. (59) studied the selective repression of V-alb coded protein (P120) on oncogene product associated with tyrosine kinase activity by N-methylisatin-4',4'-diethyl thiosemicarbazone and N-allyl-isatin-4',4'-diallyl thiosemicarbazone. These compounds selectively suppress the V-alb oncogene as well as moloney murine leukaemia virus (Fig. 28).

Broadbent et al. (60) reviewed the chemistry and pharmacology of indole-3-carbinol and 3-methoxymethyl indole; they showed antimutagenic, anticarcinogenic properties against a variety of classes of carcinogens and acted as anticancer agents against certain common neoplasms.

MISCELLANEOUS ACTIVITIES

Antitubercular activity. – Ramachandran (61) synthesized 1-nonyl-7-phenyl-1H-indol-2,3-dione and the MIC against Mycobacterium tuberculosis was ≤ 20 µg mL⁻¹.
Varma and Pandeya (62) synthesized 3-\[p-(p-(alkoxycarbonyl)-phenyl)carbamoyl)] phenyl)imino-1-aminomethyl-2-indolinones and investigated their antitubercular activity against *M. tuberculosis* H37Rv (Fig. 34).

Nine compounds have shown complete inhibition of the growth of *M. tuberculosis* H37Rv with MIC ranging from 10 to 20 μg mL\(^{-1}\).

Collino and Volpe (63) synthesized Mannich bases of isatin with dipiperidine. The synthesized compounds had fibrinolytic (5 mg kg\(^{-1}\) in mice), muscle relaxant, antiallergic, antihistaminic, immunosuppressant and antithrombotic activities.

*Inhibitor of glucose, aminoacid uptake.* – Gargari et al. (64) have shown that isatin competitively inhibited (27–40%) Na\(^+\) dependent L-Lysine uptake in rat intestine. Isatin was unaffected by SH group reacting agents. Isatin (1–10 mmol) inhibited Na\(^+\), K\(^+\)- ATP-ase in the intestine *in vitro*, but the drug had no effect on enzyme activity under *in vivo* conditions.

Hota and Acharya et al. (65) studied the possible peripheral actions of isatin. The results showed spasmogenic responses of isatin on guinea pig, rat and rabbit ileum and rat stomach fundus. Histamine induced bronchoconstriction could be antagonized by isatin. Isatin had a cardioinhibitory effect on isolated frog heart, and hypotensive, respiratory depressant and antiuretic effects; it was devoid of any effect on inflammation and gastric activities. However, the present results suggest a possible involvement of heterogenic 5-HT\(_{3}\) receptor in GI smooth muscle.

**CONCLUSIONS**

Isatin molecule is the most versatile moiety having diverse types of biological activity; exploitation of this moiety in antiviral and anticonvulsant area will be especially fruitful.

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**SAŽETAK**

Farmakološko djelovanje izatina i njegovih derivata

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Izatin je endogeni spoj prisutan u organizmu čovjeka koji posjeduje niz farmakoloških učinaka. Izatin djeluje kao antioksidans, sedativ i antikonvulziv. In vitro je snažni antagonist na receptorima za natrijeve ione u atriju. Serija p-supstituiranih semikarbazona izatina pokazala je antikonvulzivno djelovanje u MES, scPTZ i scSTY testovima, a N-Mannichove baze izatina i izatin-3-tiosemikarbazona virustatsko i tuberkulostatsko djelovanje. Metisazon je učinkovit protiv infekcija variola i vakcinia virusima. EC\textsubscript{50} N-di-metil i morfolino derivata 5-metilizatina i trimetoprima veći je od 4,3, odnosno 17,7 μg mL\textsuperscript{-1}. Izatin (3-o-nitrofenilhidrazon) inhibira rast tumorskih stanica Walker-256, a supstituirani indolinoni su aktivni protiv *M. tuberculosis* H\textsubscript{37}R\textsubscript{v} (MIC vrijednosti 10–20 μg mL\textsuperscript{-1}). Mannichove baze izatina su fibrinolitici, miorelaksansi, antihistaminici, immun-supresivi i anti trombotici, te djeluju protiv filarija. Izatin ima kardioinhibitorični učinak na srce žabe, a djeluje i kao hipotenziv, depresor respiracije i anti diuretik.

**Ključne riječi:** izatin, Mannichove baze, semikarbazoni, antikonvulzivno, antimikrobno i tuberkulostatsko djelovanje

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