Bioorganic Chemistry

http://dx.doi.org/10.7124/bc.000B15
UDC 615.31.015.4:547.789.13:004.738.52

L.M. Mosula, N.I. Vynnytska
I. Horbachevsky Ternopil National Medical University
1, Maidan Voli, Ternopil, Ukraine, 46001
mosula@tdmu.edu.ua

COMPUTATIONAL PREDICTION OF BIOLOGICAL ACTIVITY OF 5-(2-OXOINDOLIN-3-YLIDENE)-SUBSTITUTED DERIVATIVES OF 3-(BENZO[*D*]THIAZOL-2-YLAMINO)-2-THIOXOTHIAZOLIDIN-4-ONES

Aim. *To carry out in silico research of potential affinity of 5-isatinylidene derivatives of 3-(benzo[d]thiazol-2-ylamino)-2-thioxothiazolidin-4-one to biotargets and determine their possible belonging to ATC classes.* ***Methods.*** *Web tool SuperPred 3.0.* ***Results.*** *The predominant antitumour activity of the compounds was determined. The potential biological activity of derivatives 5 – 19 was compared with the in vitro efficacy of the core heterocycle, previously synthesized compounds 1 – 4 and the known effect of the antineoplastic drug Sutent (Pfizer Inc., USA). The compounds exhibited the hignest group efficiency against two targets: Cathepsin D and Casein kinase II alpha/beta (Model accuracy are 98.95 and 99.23%, respectively). The important role of the isatinylidene moiety on the biological activity of the derivatives was determined.* ***Conclusions.*** *The highest probability of structural similarity to drugs with ATC code L01XE is predicted for compound 2 (38.18%). Compounds 15 and 19 are considered potential multi-hitters. The highest affinity is predicted for compounds: 19 (99.80% to Cath-D) and 1 (93.56% to CK2). These values exceed those predicted for Sutent. The results obtained herein provide a platform for structure-based optimization of these derivatives.*

Keywords: *rhodanine, benzothiazole, 2-oxoindolin-3-ylidene, biological activity, Drug Development, SAR analysis.*

Introduction

The search for new effective and low toxic drugs to overcome the dangerous diseases, such as cancer, cardiovascular diseases, HIV/AIDS, has been a pressing issue in the last decades. According to the World Health Organisation (WHO) cancer is the second cause of death worldwide. However, the modern antineoplastic drugs have major side effects and the development of resistance remains

Citation: Mosula L.M., Vynnytska N.I. (2025) Computational prediction of biological activity of 5-(2-oxoindolin-3-ylidene)-substituted derivatives of 3-(benzo[*d*]thiazol-2-ylamino)-2-thioxothiazolidin-4-ones. *Biopolymers* & *Cell*, 2(41), 130—138. http://dx.doi.org/10.7124/bc.000B15

a problem. It encourages scientists to search for new multi-target drugs that could solve this problem [1].

Researchers have always been interested in rhodanine derivatives because of their multifaceted biological activity: antitumour, antidiabetic, anti-inflammatory, antituberculosis *etc* [2, 3]. As shown by SAR analysis, the biological activity of the derivatives of the series depends on the substituents in positions C-5 and N-3 of the rhodanine cycle [4]. The combination of the rhodanine scaffold with other pharmacophore fragments is a promising direction of research with the purpose of obtaining pharmacologically active compounds (PACs). In our previous studies, we have proven the prospects of combining rhodanine scaffold with a benzothiazole fragment in one molecule [5]. Anti-tuberculosis, antiviral, antioxidant, antitumour and other biological effects of benzothiazole derivatives are known [6, 7]. In our opinion, the introduction of an isatinylidene fragment at the position 5 of the rhodanine cycle may facilitate the discovery of new PACs with a pronounced therapeutic effect. The anticonvulsant, antitumour, antimicrobial and antioxidant effects of isatin derivatives have been known for a long time, which contributes to the widespread use of such fragments in Drug Development [8, 9]. We combined these fragments in the molecules of our derivatives for the discovery of PACs.

Aim. To carry out *in silico* research of potential affinity of 5-isatinylidene derivatives of 3-(benzo[*d*]thiazol-2-ylamino)-2-thioxothiazolidin-4-one to biotargets and determine their possible belonging to ATC (Anatomical Therapeutic Chemical Classification System) classes.

Materials and Methods

For the *in silico* research we used some earlier synthesized (compounds 1—4) with previously confirmed antitumour [5], antiviral [10] activity and virtually modelled (compounds 5—19) molecules

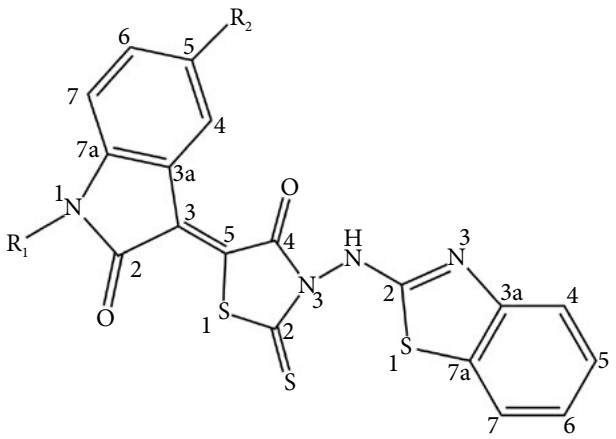


Fig. 1. 5-Isatinylidene derivatives of 3-(benzo[*d*]thiazol-2-ylamino)-2-thioxothiazolidin-4-one: 1 — R_1 = H, R_2 = H; 2 — R_1 = H, R_2 = CH_3; 3 — R_1 = H, R_2 = Br; 4 — R_1 = CH_3, R_2 = = H; 5 — R_1 = C_2H_5, R_2 = H; 6 — R_1 = *n*-C_3H_7, R_2 = H; 7 — R_1 = = *n*-C_4H_9, R_2 = H; 8 — R_1 = *i*-C_4H_9, R_2 = H; 9 — R_1 = *n*-C_5H_{11}, R_2 = H; 10 — R_1 = *i*-C_5H_{11}, R_2 = H; 11 — R_1 = CH_3, R_2 = CH_3; 12 — R_1 = C_2H_5, R_2 = CH_3; 13 — R_1 = C_2H_5, R_2 = C_2H_5; 14 — R_1 = C_2H_5, R_2 = *i*-C_3H_7; 15 — R_1 = *i*-C_3H_7, R_2 = *i*-C_3H_7; 16 — R_1 = *i*-C_3H_7, R_2 = F; 17 — R_1 = *i*-C_3H_7, R_2 = CH_2-F; 18 — R_1 = = *i*-C_3H_7, R_2 = C_2H_4-F; 19 — R_1 = *n*-C_4H_9, R_2 = C_2H_4-F

on the basis of 3-(benzo[*d*]thiazol-2-ylamino)-2-thioxothiazolidin-4-one. General structural formula of the compounds of the studied series is shown on Fig. 1.

The previous *in silico* studies on physicochemical and pharmacokinetic properties of the molecules confirmed the viability of search for biologically active compounds among the rhodanine derivatives with a benzothiazole moiety in molecules [11].

Chemistry

Chemical composition and structure of the base compound and some of its 5- isatinylidene derivatives (compounds 1—4) were determined with the elemental analysis and ^{1}H NMR spectroscopy [5]. In this work we discuss the potential of the new modelled hybrid structures (compounds 5—19) and predict possible biological activities of a whole series of derivatives.

In silico experiment

Prediction of ATC codes according to the WHO classification and targets for small molecules facilitates the process of Drug Development during the initial stages. One of such instruments is the upgraded version of SuperPred 3.0 [12, 13]. All the predictions are based on the structural similarity of new molecules to finished medicinal products (FMPs). A compound is considered a potential milti-hitter, if it is predicted to have a high probability (>1%) of belonging to certain ATC classes combined with a very high probability of binding to biological targets (>80%). The accuracy of the prediction is sufficiently high at 80.5% [14]. On this platform you can calculate quantitative indicators of the probable binding of ligands to targets (Probability in %) and determine the general accuracy of the prediction model (Model accuracy in %) [13]. Thus, the web server allows you to predict medical indications for new compounds and find binding targets for them.

Results and Discussions

We have studied the structural similarity of 5-isatinylidene derivatives with the FMPs and their ability to bind to biological targets. According to SuperPred 3.0 all the derivatives of the series have more than one indication, so they belong to several ATC classes. A group structural similarity of the derivatives of the series, with the exception of compound 8, to antineoplastic and immunomodulating agents, that are assigned code L01XE (protein kinase inhibitors), is observed. Additionally, similarity to drugs assigned code L02BB (anti-androgen hormone antagonists and related agents) is predicted for compound 16. A comparative analysis of the potential biological activity of 5-isatinylidene derivatives to the base heterocycle was carried out. The highest probability of structural similarity to antitumour drugs (L01XE) is predicted for compound 2 and is 38,18%, unlike the base compounds which is 2.59%. Other derivatives of the series are characterized by different values of the predicted similarity which ranges from 32.94% (compound 16) to 1.39% (compound 10).

SuperPred 3.0 discovered structural similarity of the studied compounds with not just antitumour MPs, but also other drugs, however, group structural similarity to FMPs with a different pharmacological activity isn't predicted. We found structural similarities between the input compounds and antineoplastic drugs (Sutent, Nintedanib, Afatinib, Dacomitinib, Cediranib, Masitinib (L01XE — Protein kinase inhibitors). Most of the derivatives (compounds 1—4, 6—19) are similar hypnotics and sedatives, assigned ATC code N05CD (benzodiazepine derivatives), and some of them (compounds 2—4, 6—19), as well as the base heterocycle, are structurally similar to other hypnotics and sedatives that are assigned ATC code N05CM. The studied derivatives are selectively similar to MPs, that intended for the treatment of the nervous system diseases: compounds 1—4, 11—13 to anxiolytics (benzodiazepine derivatives N05BA), compounds 4, 5, 7, 9, 13 to antiepileptics (carboxamide derivatives (N03AF), or succinimide derivatives (N03AD), or hydantoin derivatives (N03AB)), compounds 6—10 to antidepressants (non-selective monoamine reuptake inhibitors N06AA), compound 11 to antipsychotic drugs (diazepines, exazepines, thiazepines and oxepines N05AH), and compounds 12, 13, 16—18 to analgesics and antipyretics in ATC (N02BG). *In silico* analysis confirmed structural similarity of compounds 1 and 3 to FMPs with antiviral activity (J05AP — antivirals for treatment of HCV infections), and for compounds 7, 8 and 9, antiviral activity is expected for topical use (antivirals, topical) due to their similarity to drugs assigned ATC code D06BB. Structural similarities were found between some of the derivatives of this series and drugs intended for the treatment of cardiovascular diseases: angiotensin II receptor blockers (ARBs), plain C09CA), antiarrhythmics, class III C01BD), dermatologicals (antifungals for topical use D01AE), respiratory system drugs (phenothiazine derivatives, systemic antihistamines R06AD). Some of the derivatives

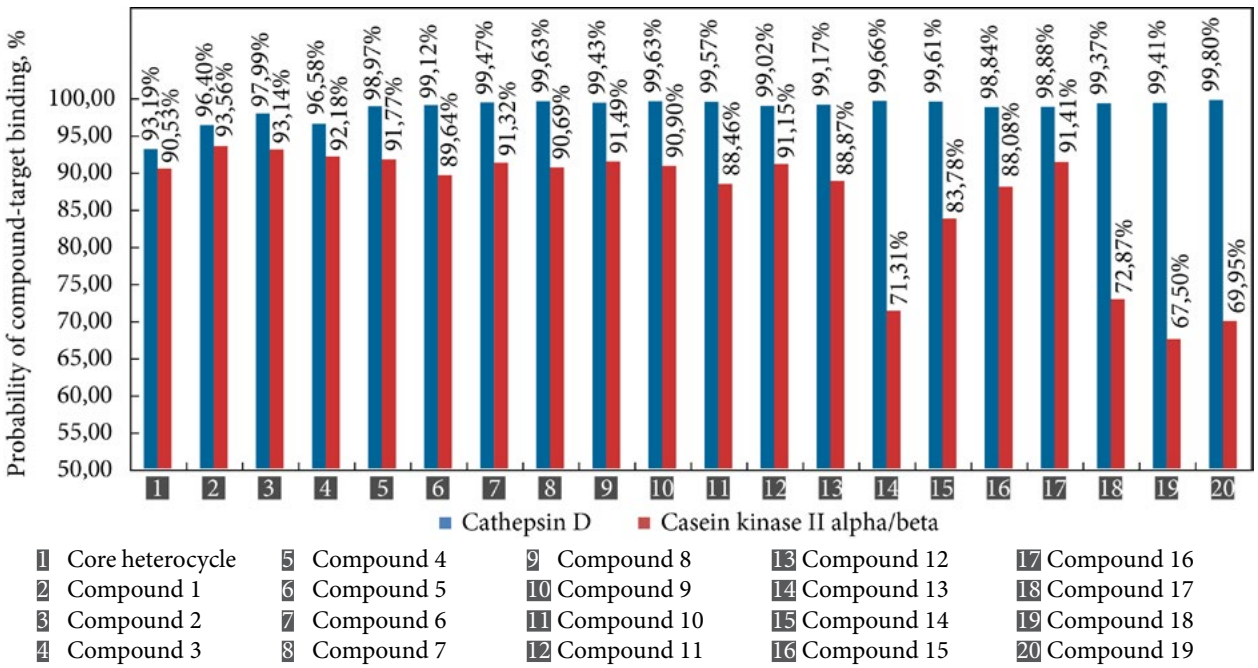


Fig. 2. The highest probability of binding of the core heterocycle and compounds 1—19 with targets for cancer therapy (in %)

have individual similarities with drugs for the treatment of the alimentary tract and metabolism, which are assigned ATC codes A06AB — contact laxatives, A03AC — synthetic antispasmodics, amides with tertiary amines for functional gastrointestinal disorders, A03AA — synthetic anticholinergics, esters with tertiary amino group for functional gastrointestinal disorders. Other derivatives are similar to musculo-skeletal system drugs (M01AC — oxicams, anti-inflammatory and antirheumatic drugs, M04AB — drugs preparations increasing uric acid excretion, M01AE — propionic acid derivatives, anti-inflammatory and antirheumatic products, M01AH — coxibs. Some compounds have structural similarities to thiouracil antithyroid preparations with ATC code H03BA.

Compound 1 with an unsubstituted isatinylidene fragment, unlike other derivatives of the series and the core heterocycle, is structurally similar to antiparasitic products, insecticides and repellents that are assigned ATC code P01AR (arsenic compounds, for amoebiasis and other protozoal diseases). Compound 6 with a propyl radical in position 1 of the isatinylidene fragment, unlike other compounds, is predicted to have similarity to MPs used in erectile dysfunction (G04BE). Upon the introduction of branched alkyl substituents into the isatinylidene fragment, structural similarity of the compounds to ophthalmological drugs, which are assigned ATC code S01XA, appears.

Compounds 15 and 19 are potential multi-hitters. For compound 15, the structural similarity to ophthalmological drugs with ATC code S01XA is predominant (63.37%), and compound 19 is most similar (62.63%) to cardiovascular system drugs (ARBs, plain C09CA).

According to the SuperPred prediction, all 19 compounds of the studied series and the core heterocycle exhibit a wide range of activity with high values of the probability of binding to targets with a significant prediction accuracy. The ability to bind to multiple targets is characteristic of all the modelled compounds. Due to the conducted study we were able to find the most promising targets for binding. Among the list of predicted targets, the targets for antitumour therapy are

predominant. We took into account the targets common to all compounds in the series with the highest binding probability (Fig. 2). The model's prediction accuracy was over 90%.

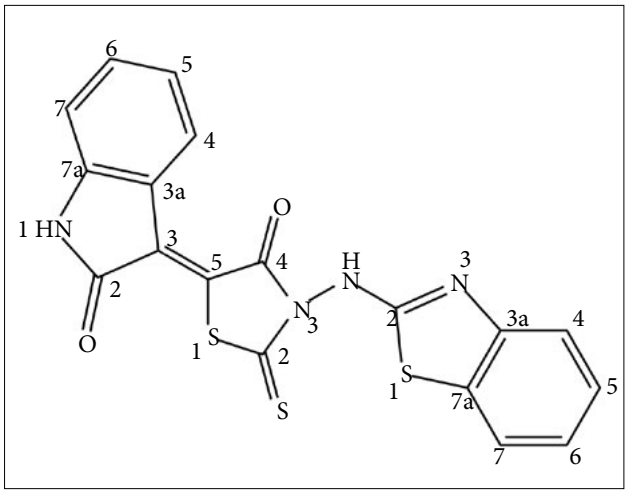
With the highest accuracy of prediction models (98.95% and 99.23%, respectively), the highest affinity of the compounds in the series is predicted for two targets: Cathepsin D and Casein kinase II alpha/beta.

Cathepsin D (Cath-D) is a type of lysosomal asparagine protease that has an integral role in protein degradation and cellular metabolism. It is a part of the A1 peptidase family and is widely expressed in various tissues (kidney, liver, brain). An abnormal expression or activity of Cath-D is linked to many diseases (such as cancer, hypertension, multiple sclerosis, Alzheimer's disease, *etc.*) The development of its inhibitors might play a key role in the death of cancer cells. Cath-D is a high-potential target for the development of anticancer drugs [15]. Our compounds are predicted to have a high probability of binding to this target ranging from 96.40% to 99.80%, which is higher than the corresponding value for the base compound (93.19%), with a prediction model accuracy of 98.95%.

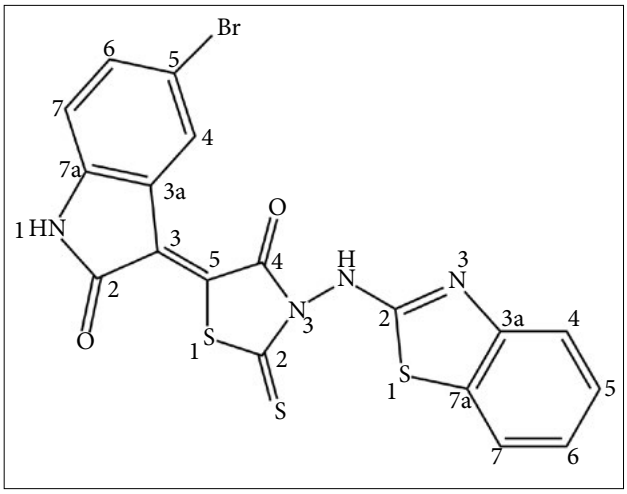
Casein kinase II (CK2) as serine/threonine kinase is a protein kinase. This kinase is a hetero-tetrameric enzyme which is classified into two catalytic subunits (α and/or α') and two regulatory subunits (β and/or β'), put into question the stability, selective control and enhancement of the enzyme activity. In addition, CK2 is an irregular kinase that is activated without any external stimuli. CK2 is primarily implicated in many diseases, cancer and cardiac hypertrophy in particular. It has been found that CK2s were implicated in cell biology and the progression of cancer, anti-apoptosis and survival support, up-regulation of oncogenes, and downregulation of tumour suppressor genes This kinase was found to overexpress in a number of cancer cell lines, including prostate, breast, colon, cholangiocarcinoma and solid cancer/tumour. Given the significant role of CK2 in tumour progression, compounds that inhibit its regulation are becoming potential chemotherapeutic agents [16]. The probability of inhibition of this target by the derivatives of the series ranges from 67.50% (compound 18) to 93.56% (compound 1) with a high accuracy of the prediction model (99.23%). The probability of binding of the base compound to this target is 90.53%.

Aside from the aforementioned targets, affinity for other targets responsible for the growth and development of cancer cells is also predicted: Signal transducer and activator of transcription 3 (STAT-3) (brain cancer, chronic lymphocytic leukaemia, hepatocellular carcinoma, multiple myeloma, recurrent glioblastoma, solid tumour/cancer), DNA-(apurinic or apyrimidinic site) lyase (DNA AP lyase) (glioma, melanoma, ocular cancer, solid tumour/cancer), DNA topoisomerase I (TOP1-DNA) (acute lymphoblastic leukaemia, bladder cancer, breast cancer, colorectal cancer, esophageal cancer, gastric adenocarcinoma, glioblastoma multiforme, lung cancer, lymphoma, metastatic colorectal cancer, myelodysplastic syndrome, ovarian cancer, renal cell carcinoma, small-cell lung cancer, solid tumour/cancer), Aldose reductase (AR) (head and neck cancer), *etc.* The probability of binding of the series derivatives to these targets is somewhat lower and ranges from 54.12 to 95.71%.

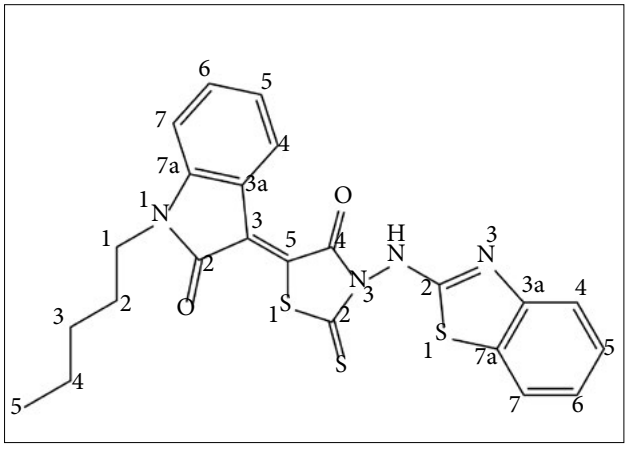
We have carried out a comparative analysis of the potential biological activity of new compounds 5—19 with determined *in vitro* types of activity for core heterocycle, previously synthesized compounds 1—4 and the known action of the antineoplastic drug Sutent (*Pfizer Inc., USA*), which also contains a 2-oxoindolin-3-ylidene moiety in the molecule of the active substance sunitinib malate. Sutent is a treatment for: kidney cancer (Renal cell carcinoma, RCC) that has spread to other parts of the body (advanced or metastatic) a rare type of sarcoma called gastrointestinal stromal tumours (GISTs), pancreatic neuroendocrine tumors (PNETs). It works by inhibiting multiple protein kinases involved in tumor growth and blood vessel formation. The synthesized compounds also showed *in vitro* moderate effects on kidney cancer cell lines.



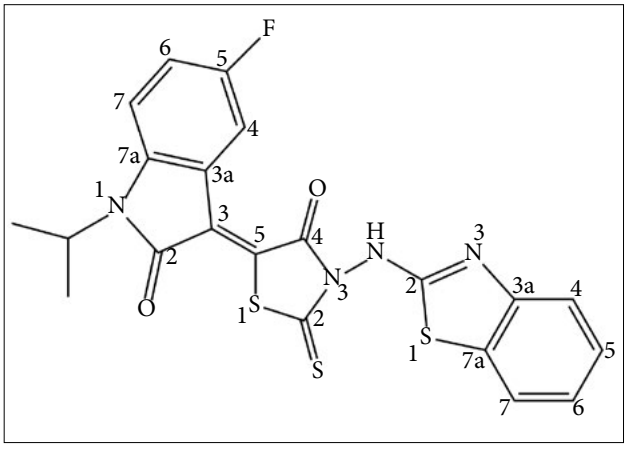
a



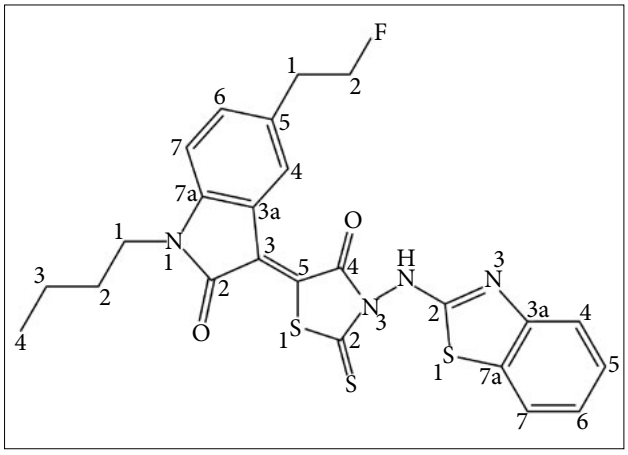
b



c



d



e

Fig. 3. Chemical structures of the compounds with the highest predicted affinity values to anti-tumour targets: *a* — compound 1 (93.56% to CK2); *b* — compound 3 (94.90% to DNA AP lyase and 89.28% to AR); *c* — compound 9 (88.07% to TOP1-DNA); *d* — compound 16 (95.71% to STAT-3), *e* — compound 19 (99.80% to Cath-D)

Among the predicted common targets of our compounds and Sutent with a high probability are: Cath-D, CK2, DNA AP lyase. The hit compounds 19, 1, 3 are predicted to have higher affinity to these targets than Sutent. Potential probability of Sutent binding to such targets is respectively: 98.39%, 85,22%, 82.40%.

The *in silico* prediction confirmed the detected *in vitro* and *in vivo* antitumour and antiviral activity of compounds 1 and 3. According to the prediction results, some of the modelled derivatives (compounds 7, 8, 9), as well as earlier synthesized compounds 1 and 3, have a polyprofile character, i.e., they are characterised by a sufficient probability of binding to targets associated with viral and cancer diseases. Thus, compounds 1, 3, 7, 8, 9, in addition to potentially high antitumour activity, are characterised by a binding probability of >75% to targets associated with viral diseases: Dual-specificity tyrosine-phosphorylation regulated kinase 1A (DYRK1A) (synechialgalovirus disease), DNA topoisomerase I (TOP1-DNA) (acquired immune deficiency syndrome, human immunodeficiency virus infection). Additionally, with a slightly lower probability (about 70%), the compounds, except for compound 8, may affect two other targets responsible for the development of viral diseases: Adenosine A3 receptor (A3AR) (hepatitis C virus infection) and Toll-like receptor 8 (TLR8) (herpes simplex virus infection).

The analysis of the relationship 'chemical structure — biological activity' in a number of the studied derivatives allows us to state a significant influence of the isatinylidene fragment in the structure of molecules on the expression of their biological activity. Upon the introduction of an isatinylidene fragment at the position 5 of the base heterocycle, the probability of binding of compounds to most targets increases. The affinity of the compounds of the series to the targets depends on the substituents introduced in the isatinylidene fragment and their position in the cycle. It is determined that the modification of N1 and C5 positions of the isatinylidene cycle has a crucial influence on the antitumour effect. Thus, the introduction of halogens (Br, F) promotes affinity for therapeutic targets. This is reflected in the predicted values of structural similarity to antineoplastic agents and the values of binding affinity to the corresponding targets. The most optimal in this context is the presence of radicals at positions 1 and 5 of the isatinylidene fragment: R_1 = H and R_2 = H (compound 1), R_1 = H and R_2 = Br (compound 3), R_1 = *n*-C_5H_{11} and R_2 = H (compound 9), R_1 = *i*-C_3H_7 and R_2 = F (compound 16), R_1 = *n*-C_4H_9 and R_2 = = C_2H_4-F (compound 19). The structural formulas of compounds with the highest probability of binding to the therapy targets are shown on Fig. 3.

Conclusions

SuperPred 3.0 prediction confirmed the detected *in vitro* antitumour and antiviral effects of the earlier synthesized compounds and revealed a wide therapeutic potential of the new modelled derivatives of the series. Among them, two potential multi-hitters were identified — compounds 15 and 19. The predominant antitumour activity of the studied compounds is predicted. This is evidenced by the group structural similarity, with the exception of compound 8, to antineoplastic and immunomodulating agents, which are assigned the code L01XE (protein kinase inhibitors, antineoplastic drugs). The affinity of the derivatives of this series to multiple targets that are responsible for the growth and development of cancer cells is predicted: Cath-D, CK2, STAT-3, DNA AP lyase, TOP1-DNA, AR, *etc.* With the highest accuracy of the prediction models (near 100%), the highest probability of binding to targets is predicted for compounds: 19 (99.80% to Cath-D) and 1 (93.56% to CK2). These values are higher than the probable affinity values of core heterocycle and antineoplastic drug Sutent. For compounds 1, 3, 7—9, besides the high binding affinity (Probability >90%) to common antitumour targets, sufficient affinity (Probability >75%) to DYRK1A and TOP1-DNA targets, which affect the course of viral diseases, is predicted. For potentially active compounds it is advisable to conduct thorough *in vitro* and *in vivo* studies.

Conflicts of Interest. The authors declare no conflict of interest.

REFERENCES

1. *Ali BS, Mohammed AF, Kariuki BM, et al., and H M Abdu-Allah H.* Tetrahydrocarbazoles incorporating 5-arylidene-4-thiazolinones as potential antileukemia and antilymphoma targeting tyrosine kinase and tubulin polymerase enzymes: Design, synthesis, structural, biological and molecular docking studies. *Bioorg Chem.* 2024; **153**:107817.
2. *Sahiba N, Sethiya A, Soni J, et al., and Agarwal S.* Saturated Five-Membered Thiazolidines and Their Derivatives: From Synthesis to Biological Applications. *Top Curr Chem (Cham).* 2020; **378**(2):34.
3. *Shepeta YL, Lozynskyi AV, Tomkiv ZV, et al., and Lesyk RB.* Synthesis and evaluation of biological activity of rhodanine-pyrazoline hybrid molecules with 2-(2,6-dichlorophenylamino)-phenylacetamide fragment. *Biopolym Cell.* 2020; **36**(2):133—45.
4. *Chaurasyia A, Chawla P, Monga V, Singh G.* Rhodanine derivatives: An insight into the synthetic and medicinal perspectives as antimicrobial and antiviral agents. *Chem Biol Drug Des.* 2023; **101**(3):500—49.
5. *Mosula L, Zimenkovsky B, Havrylyuk D, et al., and Lesyk R.* Synthesis and antitumor activity of novel 2-thioxo-4-thiazolidinones with benzothiazole moieties. *Farmacia.* 2009; **57**(3):321—30.
6. *Yadav KP, Rahman MA, Nishad S, et al., and Mujahid M.* Synthesis and biological activities of benzothiazole derivatives: A review. *Intelligent Pharmacy.* 2023; **1**(3):122—32.
7. *Sumit, Kumar A, Mishra AK.* Advancement in Pharmacological Activities of Benzothiazole and its Derivatives: An Up to Date Review. *Mini Rev Med Chem.* 2021; **21**(3):314—35.
8. *Beula SJ, Reddy TRM, Suthakaran R, Suneetha K.* A Review an Isatin, Isatin Derivatives and their Pharmacological Activity. *RJPPD.* 2021; **13**(2):59—72.
9. *Cheke RS, Patil VM, Firke SD, et al., and Snoussi M.* Therapeutic Outcomes of Isatin and Its Derivatives against Multiple Diseases: Recent Developments in Drug Discovery. *Pharmaceuticals (Basel).* 2022; **15**(3):272.
10. *Mosula LM.* Antiviral activity of 3-benzothiazole substituted 4-thiazolidinone derivatives. *Pharm Rev.* 2012; **3**:22—6.
11. *Mosula LM, Vynnytska NI, Mosula VS.* Molecular design and predictive evaluation of the properties of the series compoundsof 5-(2-oxoindolin-3-ylidene) substituted derivatives of 3-(benzo[d]thiazol-2-ylamino)-2-thioxo-thiazolidin-4-one. *Art Med.* 2025; **33**(1):77—81.
12. SuperPred 3.0. Available online: https://prediction.charite.de/index.php/ (accessed on 10 February 2025).
13. *Gallo K, Goede A, Preissner R, Gohlke BO.* SuperPred 3.0: drug classification and target prediction-a machine learning approach. *Nucleic Acids Res.* 2022; **50**(W1):W726–W31.
14. *Kopak NA.* Searching of biological activity of s-esters 4- acetylaminobenzenethiosulfoacid using methods of chemoinformatics. *CTAS.* 2023; **6**(2):76—86.
15. *Seo SU, Woo SM, Im SS, et al., and Kwon TK.* Cathepsin D as a potential therapeutic target to enhance anticancer drug-induced apoptosis via RNF183-mediated destabilization of Bcl-xL in cancer cells. *Cell Death Dis.* 2022; **13**(2):115.
16. *Peytam F, Emamgholipour Z, Mousavi A, et al., and Foroumadi A.* Imidazopyridine-based kinase inhibitors as potential anticancer agents: A review. *Bioorg Chem.* 2023; **140**:106831.

Received 16.04.2025

Л.М. Мосула, Н.І. Винницька
Тернопільський національний медичний університет
імені І.Я. Горбачевського
Майдан Волі, 1, Тернопіль, Тернопільська область, 46001
mosula@tdmu.edu.ua

ОБЧИСЛЮВАЛЬНЕ ПРОГНОЗУВАННЯ БІОЛОГІЧНОЇ АКТИВНОСТІ
РЯДУ 5-(2-ОКСОІНДОЛІН-3-ІЛІДЕН)-ЗАМІЩЕНИХ ПОХІДНИХ
3-(БЕНЗО[*d*]ТІАЗОЛ-2-ІЛАМІНО)-2-ТІОКСОТІАЗОЛІДИН-4-ОНУ

Мета. Провести *in silico* дослідження потенційної афінності 5-ізатиніліденпохідних 3-(бензо[*d*]тіазол-2-іламіно)-2-тіоксотіазолідин-4-ону до біомішеней та встановити їх можливу приналежність до АТС класів. ***Методи.*** Веб-інструмент SuperPred 3.0. ***Результати.*** Встановлено переважаючу протипухлинну дію сполук.

Потенційну біологічну активність похідних 5—19 порівнювали з ефективністю *in vitro* основного гетероциклу, раніше синтезованих сполук 1—4 та відомою дією антинеопластичного препарату «Сутент» (Pfizer Inc., США). Сполуки показали найвищу групову ефективність стосовно двох мішеней**:** Cathepsin D і Casein kinase II alpha/beta (точність моделей прогнозування 98,95 і 99,23%, відповідно). Встановлено важливу роль ізатиніліденового фрагмента на вияв біологічної активності похідних. ***Висновки.*** Найвищу ймовірність структурної схожості з протипухлинними препаратами під АТС кодом L01XE прогнозовано для сполуки 2 (38,18%). Сполуки 15 і 19 вважаються потенційними мультихітерами. Найвища афінність передбачається для сполук**:** 19 (99,80% до Cath-D) і 1 (93,56% до CK2). Ці значення перевищують прогнозовані для «Сутент». Одержані результати створюють платформу для структурної оптимізації цих похідних.

Ключові слова**:** роданін, бензотіазол, 2-оксоіндолін-3-іліден, біологічна активність, створення ліків, аналіз «структура — дія».