Integrated in silico profiling of N-methyl 1,2,4-triazole derivatives against wound-healing-related molecular targets

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Wound healing is a complex biological process involving coordinated hemostatic, inflammatory, proliferative, and remodeling responses. The simultaneous involvement of multiple molecular pathways provides a rationale for multi-target computational screening as an approach to identify compounds with complementary molecular recognition profiles.

The aim of the work was to evaluate the multi-target potential of a series of *N*-methyl derivatives toward molecular targets associated with different stages of wound healing and to identify promising compounds by integrating molecular docking, protein-ligand interaction analysis, and predicted physicochemical and ADMET properties.

Materials and methods. Nineteen *N*-methyl derivatives were evaluated using SwissADME and ADMETlab 3.0. Molecular docking was performed with smina 2020.12.10 against human thrombin (PDB ID: 1DWC), 5-lipoxygenase (5-LOX; 6N2W), VEGFR-2 (3VHE), and MMP-2 (8H78), representing hemostasis, inflammation, proliferation / angiogenesis, and extracellular-matrix remodeling, respectively. Ligands were prepared using Open Babel 3.1.1. Protein-ligand interactions were characterized using PLIP.

Results. The investigated derivatives demonstrated distinct target-dependent docking and physicochemical profiles. Compound 12 showed the most favorable thrombin docking score (-7.78 kcal/mol), whereas 16 exhibited the strongest predicted interaction with 5-LOX (-8.61 kcal/mol). Compound 18 was the highest-ranking compound against MMP-2 (-8.25 kcal/mol), while 19 showed the most favorable VEGFR-2 score (-8.48 kcal/mol) and the strongest overall four-target docking profile (mean -8.12 kcal/mol). Interaction analysis revealed different combinations of hydrogen-bonding and hydrophobic contacts without direct ligand-metal coordination in the prioritized 5-LOX and MMP-2 complexes. Integration with physicochemical and ADMET predictions identified distinct advantages and limitations among the leading compounds.

Conclusions. Compounds 16, 18, and 19 demonstrated complementary multi-target profiles across wound-healing-related molecular targets. Compound 16 showed a comparatively balanced computational profile, 18 combined favorable 5-LOX/MMP-2 recognition with predicted solubility, and 19 exhibited the strongest overall docking profile but additional predicted permeability and safety liabilities. These compounds represent rational candidates for subsequent experimental validation.

Keywords: wound healing, N-methyl derivatives, molecular docking, multi-target screening, thrombin, 5-lipoxygenase, VEGFR-2, MMP-2, ADMET.

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Інтегроване in silico профілювання N-метилпохідних 1,2,4-тріазолу щодо молекулярних мішеней, пов'язаних із загоєнням ран

Ю. В. Карпенко, О. С. Глух

Загоєння ран є складним біологічним процесом, що включає взаємопов'язані гемостатичні, запальні, проліферативні та ремоделювальні реакції. Одночасна участь численних молекулярних шляхів обґрунтовує застосування мультитаргетного комп'ютерного скринінгу для пошуку сполук із комплементарними профілями молекулярного розпізнавання.

Мета роботи – оцінити мультитаргетний потенціал серії *N*-метильних похідних щодо молекулярних мішеней, пов'язаних із різними стадіями загоєння ран, та визначити перспективні сполуки шляхом інтеграції молекулярного докінгу, аналізу білок-лігандних взаємодій і прогнозованих фізико-хімічних та ADMET-характеристик.

Матеріали і методи. Досліджено 19 *N*-метильних похідних із використанням SwissADME та ADMETlab 3.0. Молекулярний докінг виконували за допомогою smina 2020.12.10 щодо тромбіну людини (PDB ID: 1DWC), 5-ліпоксигенази (5-LOX; 6N2W), VEGFR-2

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Keywords: wound healing, N-methyl derivatives, molecular docking, multi-target screening, thrombin, 5-lipoxygenase, VEGFR-2, MMP-2, ADMET.

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(3VHE) та MMP-2 (8H78), які представляють гемостаз, запалення, проліферацію / ангіогенез і ремоделювання позаклітинного матриксу відповідно. Ліганди готували за допомогою Open Babel 3.1.1, а білок-лігандні взаємодії аналізували з використанням PLIP.

Результати. Досліджені похідні характеризувалися вираженими таргет-залежними відмінностями. Сполука 12 мала найсприятливіший результат докінгу щодо тромбіну (-7,78 ккал/моль), 16 – щодо 5-LOX (-8,61 ккал/моль), 18 – щодо MMP-2 (-8,25 ккал/моль), а 19 – щодо VEGFR-2 (-8,48 ккал/моль). Сполука 19 також характеризувалася найсприятливішим середнім результатом для чотирьох мішеней (-8,12 ккал/моль). Аналіз взаємодій дав змогу встановити різні комбінації водневих і гідрофобних контактів без прямої координації лігандів із металами у пріоритетних комплексах 5-LOX та MMP-2. Інтеграція результатів із прогнозами фізико-хімічних та ADMET-властивостей виявила специфічні переваги й обмеження провідних сполук.

Висновки. Сполуки 16, 18 і 19 мали комплементарні мультитаргетні профілі. Сполука 16 характеризувалась порівняно збалансованим обчислювальним профілем, 18 поєднувала сприятливе розпізнавання 5LOX/MMP-2 із прогнозованою розчинністю, а 19 мала найсильніший загальний докінговий профіль, але додаткові прогнозовані обмеження проникності та безпеки. Визначені сполуки є обґрунтованими кандидатами для подальшої експериментальної валідації.

Ключові слова: загоєння ран, N-метильні похідні, молекулярний докінг, мультитаргетний скринінг, тромбін, 5-ліпоксигеназа, VEGFR-2, MMP-2, ADMET.

Актуальні питання фармацевтичної і медичної науки та практики. 2026. Т. 19, № 3(52). С. 231-238

Wound healing is a coordinated biological process involving overlapping phases of hemostasis, inflammation, proliferation, and remodeling and complex interactions among immune and resident cells, extracellular-matrix components, proteolytic enzymes, and signaling mediators [1,2]. Disruption of their spatial and temporal regulation may lead to persistent inflammation, impaired angiogenesis, excessive matrix degradation, and delayed re-epithelialization [1]. The multifactorial nature of wound repair therefore provides a rationale for multi-target drug discovery, in which structurally related compounds are evaluated against several biologically relevant proteins rather than within a strictly single-target framework [3,4,5]. Importantly, multi-target recognition should not be interpreted as indiscriminate inhibition, because the functional consequences of ligand binding depend on the biological role of each target and the stage of tissue repair [3,4].

Four proteins representing complementary wound-healing-related processes were selected for the present study. Thrombin, a central serine protease of coagulation, contributes to fibrin formation and platelet activation during hemostasis and can additionally influence cellular responses through protease-activated receptors [1,6,7,8]. During inflammation, 5-lipoxygenase (5-LOX) generates leukotriene mediators, and experimental modulation of this pathway has been associated with reduced inflammation and improved cutaneous wound closure [9]. VEGF/VEGFR-2 signaling is a major regulator of endothelial-cell proliferation, migration, and angiogenesis during the proliferative phase, supporting restoration of the wound microvasculature [1,10,11]. During remodeling, matrix metalloproteinases regulate extracellular-matrix turnover, while excessive proteolytic activity is associated with chronic non-healing wounds [12,13]. MMP-2 was therefore included as a representative zinc-dependent enzyme involved in matrix remodeling. Accordingly, thrombin, 5-LOX, VEGFR-2, and MMP-2 constitute a complementary molecular panel representing hemostatic, inflammatory, angiogenic, and remodeling-associated processes, respectively, without implying that inhibition of all four targets would necessarily promote wound healing.

Accordingly, the four selected molecular targets provide a complementary computational panel representing key functional processes across the major stages of wound healing *(Fig. 1)*.

The identification of compounds capable of recognizing such structurally and functionally diverse proteins can be facilitated by computational approaches. Molecular docking is an established structure-based method for predicting plausible ligand orientations within protein binding regions and comparing molecular recognition among structurally related compounds [14]. It has also become increasingly useful for target profiling, polypharmacology, structure–activity relationship analysis, and early-stage compound prioritization [14]. However, docking scores alone cannot adequately characterize drug-development potential because favorable protein recognition may coexist with limited solubility or permeability, extensive protein binding, metabolic liabilities, or toxicity alerts. Integration of docking with physicochemical, drug-likeness, pharmacokinetic, and toxicity predictions therefore provides a more informative framework for prioritizing compounds before experimental investigation [15,16].

Systematic analysis of structurally related chemical series is particularly valuable in this context because relatively small molecular modifications can alter lipophilicity, polarity, hydrogen-bonding capacity, solubility, and complementarity with individual protein environments. Comparison within a common scaffold can therefore reveal both target-specific structure-activity relationships and compounds with more broadly distributed molecular recognition profiles. The *N*-methyl derivatives investigated in the present study constitute such a structurally related series and provide an opportunity to evaluate how molecular variation affects predicted interactions with proteins representing different functional components of wound repair.

Aim

The aim of this work was to evaluate the multi-target potential of a series of *N*-methyl derivatives toward molecular targets associated with different stages of wound healing by integrating molecular docking and protein-ligand interaction analysis with predicted physicochemical, drug-likeness, pharmacokinetic, and toxicity profiles, and to identify the most promising compounds for subsequent experimental validation.

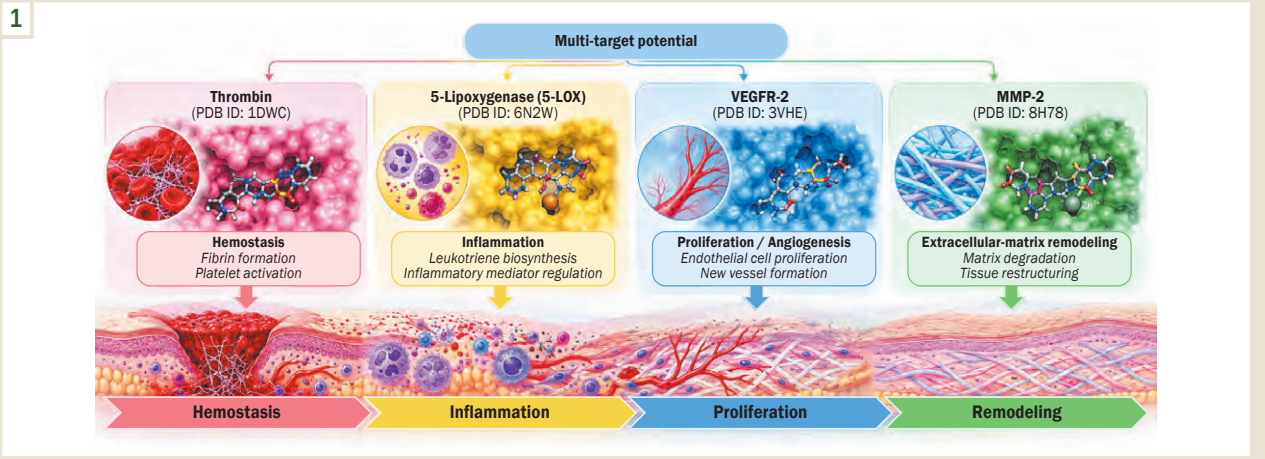


Fig. 1. Multi-target concept of the investigated molecular hybrids across the major stages of wound healing.

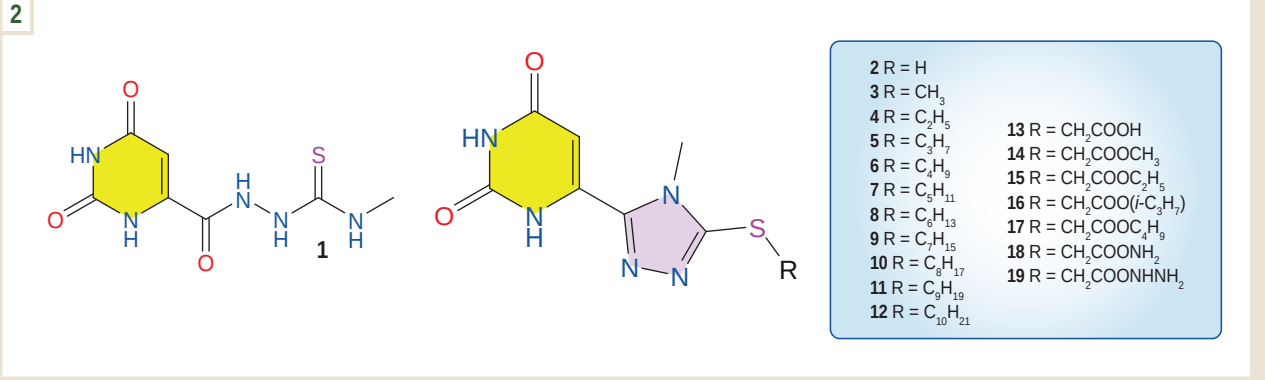


Fig. 2. Molecular hybrids as potential multifunctional wound healing agents.

Materials and methods

The computational study included 19 structurally related *N*-methyl derivatives *(Fig. 2)* and comprised physicochemical and drug-likeness assessment, ADMET prediction, multi-target molecular docking, and protein-ligand interaction analysis.

Physicochemical properties and drug-likeness were evaluated using SwissADME (Swiss Institute of Bioinformatics, Lausanne, Switzerland; accessed September 2026). Additional absorption, distribution, metabolism, excretion, and toxicity parameters were predicted using ADMETlab 3.0 (accessed September 2026).

Molecular docking was performed against four proteins representing molecular processes associated with different stages of wound repair: human thrombin (PDB ID: 1DWC; hemostasis), 5-lipoxygenase (5-LOX; PDB ID: 6N2W; inflammation), vascular endothelial growth factor receptor 2 kinase domain (VEGFR-2; PDB ID: 3VHE; proliferation / angiogenesis), and matrix metalloproteinase-2 (MMP-2; PDB ID: 8H78; extracellular-matrix remodeling). Experimentally determined protein structures were obtained from the RCSB Protein Data Bank.

Receptors were inspected before docking, non-essential solvent and heteroatomic components were removed, and catalytically relevant metal ions were retained, including the Fe-containing environment of 5-LOX and the Zn^{2+} ions of MMP-2. Ligands were prepared using Open Babel 3.1.1, with protonation states generated at pH 7.4, hydrogen atoms added, and the resulting structures converted to PDBQT format. An identical preparation procedure was applied to all compounds. Molecular docking calculations were performed using smina 2020.12.10 (based on AutoDock Vina 1.1.2) with a Vina-compatible scoring function [17]. Receptors were treated as rigid, whereas ligand torsional flexibility was retained.

The search region for each target was defined from the experimentally characterized binding region using the corresponding co-crystallized native ligand as the AutoBox reference, with an AutoBox extension of 16 Å. To characterize the overall multi-target profile, the arithmetic mean of the four target-specific docking scores was calculated for each compound and used solely as a descriptive comparative parameter rather than as a thermodynamic or pharmacological index.

Protein-ligand interactions in representative high-ranking complexes were subsequently characterized using the Protein-Ligand Interaction Profiler (PLIP) [18], with particular attention to hydrogen bonds, hydrophobic contacts, interacting amino-acid residues, and interaction geometry. Physicochemical, ADMET, docking, and interaction data were integrated for comparative compound prioritization.

Table 1. Predicted physicochemical properties of the *N*-methyl derivatives

Compound	MW, g/mol	TPSA, Å²	Consensus logP	ESOL logS	GI absorption	Bioavailability score
1	243.24	150.97	-0.92	-2.03	Low	0.55
2	225.23	135.23	-0.41	-2.54	Low	0.55
3	239.25	121.73	-0.06	-2.75	High	0.55
4	253.28	121.73	0.21	-2.97	High	0.55
5	267.31	121.73	0.62	-3.30	High	0.55
6	281.33	121.73	0.93	-3.52	High	0.55
7	295.36	121.73	1.16	-3.86	High	0.55
8	309.39	121.73	1.65	-4.20	High	0.55
9	323.41	121.73	2.00	-4.55	High	0.55
10	337.44	121.73	2.37	-4.89	High	0.55
11	351.47	121.73	2.68	-5.24	High	0.55
12	365.49	121.73	3.08	-5.59	High	0.55
13	283.26	159.03	-0.74	-2.55	Low	0.11*
14	297.29	148.03	-0.35	-2.76	Low	0.55
15	311.32	148.03	0.07	-2.99	Low	0.55
16*	325.34*	148.03*	0.33*	-3.34*	Low*	0.55*
17	339.37	148.03	0.70	-3.56	Low	0.55
18*	282.28*	164.82*	-0.99*	-2.14*	Low*	0.55*
19*	297.29*	176.85*	-1.49*	-1.93*	Low*	0.55*

MW: molecular weight; **TPSA:** topological polar surface area; **logP:** logarithm of the octanol/water partition coefficient; **ESOL logS:** predicted aqueous solubility expressed as log(mol/L); **GI:** gastrointestinal; **PAINS:** pan-assay interference compounds. Predictions were obtained using SwissADME. Asterisk (*) indicates compounds subsequently prioritized in the integrated multi-target analysis.

Results

Physicochemical and ADMET profiles. The physicochemical and drug-likeness characteristics of the 19 *N*-methyl derivatives predicted using SwissADME are summarized in *Table 1*. Molecular weights ranged from 225.23 Da to 365.49 Da, consensus logP values from -1.49 to 3.08, and TPSA values from 121.73 Å² to 176.85 Å². All compounds complied with Lipinski's rule of five and showed no PAINS alerts.

Multi-target molecular docking. Docking scores for the 19 *N*-methyl derivatives against thrombin, 5-LOX, VEGFR-2, and MMP-2 are summarized in *Table 2*. Binding was strongly target- and structure-dependent, and **16**, **18**, and **19** emerged as the principal multi-target candidates.

For thrombin, docking scores ranged from -6.60 to -7.78 kcal/mol, with **12** showing the most favorable value (-7.78 kcal/mol), followed by **19** (-7.65 kcal/mol) and **16** (-7.64 kcal/mol). The favorable thrombin score of **12** paralleled its increased lipophilicity and reduced predicted aqueous solubility.

The strongest docking scores were generally observed for 5-LOX. Compound **16** ranked first (-8.61 kcal/mol), followed by **18** (-8.42 kcal/mol), **19** (-8.28 kcal/mol), and **15** (-8.26 kcal/mol). For VEGFR-2, **19** showed the most favorable score (-8.48 kcal/mol), followed by **16** (-8.04 kcal/mol). MMP-2 produced a different ranking, with **18** (-8.25 kcal/mol) and **19** (-8.08 kcal/mol) as the leading compounds.

The arithmetic mean of the four target-specific scores was used solely as a descriptive indicator of multi-target recognition. Compound **19** showed the most favorable mean score (-8.12 kcal/mol), followed by **18** (-7.93 kcal/mol) and **16** (-7.88 kcal/mol). Thus, **16** was distinguished primarily by its strong 5-LOX recognition, **18** by the combined 5-LOX/MMP-2 profile, and **19** by consistently favorable docking across all four targets.

PLIP analysis was performed for representative high-ranking complexes to characterize the molecular interactions underlying the docking results *(Fig. 3)*.

The thrombin complex of **12** was stabilized predominantly by hydrophobic contacts with Leu99, Ile174, and Trp215, consistent with its comparatively high lipophilicity. In contrast, **19** formed hydrogen-bonding interactions involving His57 and Ser195 within the thrombin catalytic region, demonstrating that comparable docking scores can arise from different molecular recognition patterns.

For 5-LOX, **16** showed a hydrophobic contact with Arg520, whereas **18** formed a hydrogen bond involving Arg518. No direct ligand coordination with the catalytic Fe ion was detected for the prioritized compounds. In VEGFR-2, **19** formed a hydrogen bond with Lys920, while **16** was stabi-

Table 2. Molecular docking scores of the *N*-methyl derivatives against wound-healing-related molecular targets

Compound	Thrombin (1DWC)	5-LOX (6N2W)	VEGFR-2 (3VHE)	MMP-2 (8H78)	Mean
1	-6.65	-7.40	-6.72	-7.42	-7.05
2	-6.62	-7.07	-7.24	-5.51	-6.61
3	-6.64	-6.95	-7.26	-5.99	-6.71
4	-6.60	-7.55	-7.52	-5.68	-6.84
5	-6.85	-7.50	-7.62	-5.50	-6.87
6	-7.16	-7.58	-7.63	-7.55	-7.48
7	-7.48	-8.20	-7.81	-6.29	-7.44
8	-7.53	-7.75	-7.63	-6.60	-7.38
9	-7.29	-7.70	-7.70	-6.71	-7.35
10	-7.34	-7.82	-7.71	-7.03	-7.48
11	-7.37	-7.99	-7.78	-7.04	-7.55
12	-7.78*	-7.19	-7.82	-6.72	-7.38
13	-7.12	-7.86	-7.64	-7.04	-7.42
14	-7.13	-7.61	-7.83*	-7.84*	-7.60
15	-7.26	-8.26	-7.60	-7.02	-7.53
16*	-7.64*	-8.61*	-8.04*	-7.23*	-7.88*
17	-7.39	-7.69	-7.64	-6.91	-7.41
18*	-7.25*	-8.42*	-7.81*	-8.25*	-7.93*
19*	-7.65*	-8.28*	-8.48*	-8.08*	-8.12*

Scores are in kcal/mol; more negative values indicate more favorable predicted binding. Mean = arithmetic mean of the four docking scores and is used only as a descriptive multi-target parameter. Heatmap: blue = weaker, orange-red = stronger predicted docking. Asterisk (*) indicates top-ranked interactions and prioritized multi-target compounds 16, 18, and 19.

lized predominantly through hydrophobic contacts involving Leu840 and Phe918.

Compounds **18** and **19** showed the most favorable MMP-2 docking scores. Compound **19** formed a hydrogen bond with Leu138, whereas no direct ligand–Zn^{2+} coordination was identified for either compound. Thus, the favorable MMP-2 scores were associated with noncovalent recognition within the binding region rather than direct metal chelation.

Overall, the interaction analysis confirmed distinct target-dependent recognition patterns. Compound **16** combined favorable hydrophobic recognition in several targets with the strongest 5-LOX docking; **18** showed a profile weighted toward 5-LOX and MMP-2; and **19** formed hydrogen-bonding interactions in several protein environments and displayed the broadest overall docking profile. These differences support their prioritization as complementary rather than interchangeable multi-target candidates.

Discussion

The present study demonstrated that structural variation within the investigated *N*-methyl series generated distinct target-dependent molecular recognition and physicochemical profiles. A clear structure-property relationship was observed among compounds **3**–**12**, where increasing lipophilicity was accompanied by reduced predicted aqueous solubility and, for several higher homologues, improved thrombin recognition. Compound **12**, which showed the most favorable thrombin docking score, exemplified this trade-off: enhanced target-specific recognition was accompanied by less favorable solubility-related properties and did not translate into a balanced multi-target profile. Thus, optimization within this series cannot be based on docking affinity alone.

The integrated analysis highlighted compounds **16** and **19** as the most informative multi-target candidates. Compound **16** showed the strongest predicted recognition of 5-LOX (-8.61 kcal/mol) while maintaining favorable interactions with thrombin and VEGFR-2. Importantly, these docking characteristics were accompanied by a comparatively balanced physicochemical and predicted ADMET profile, although P-glycoprotein inhibition and DILI alerts require experimental clarification. Compound **19** displayed the strongest overall multi-target recognition, including the most favorable VEGFR-2 score (-8.48 kcal/mol) and the best mean score across the four targets (-8.12 kcal/mol). However, its

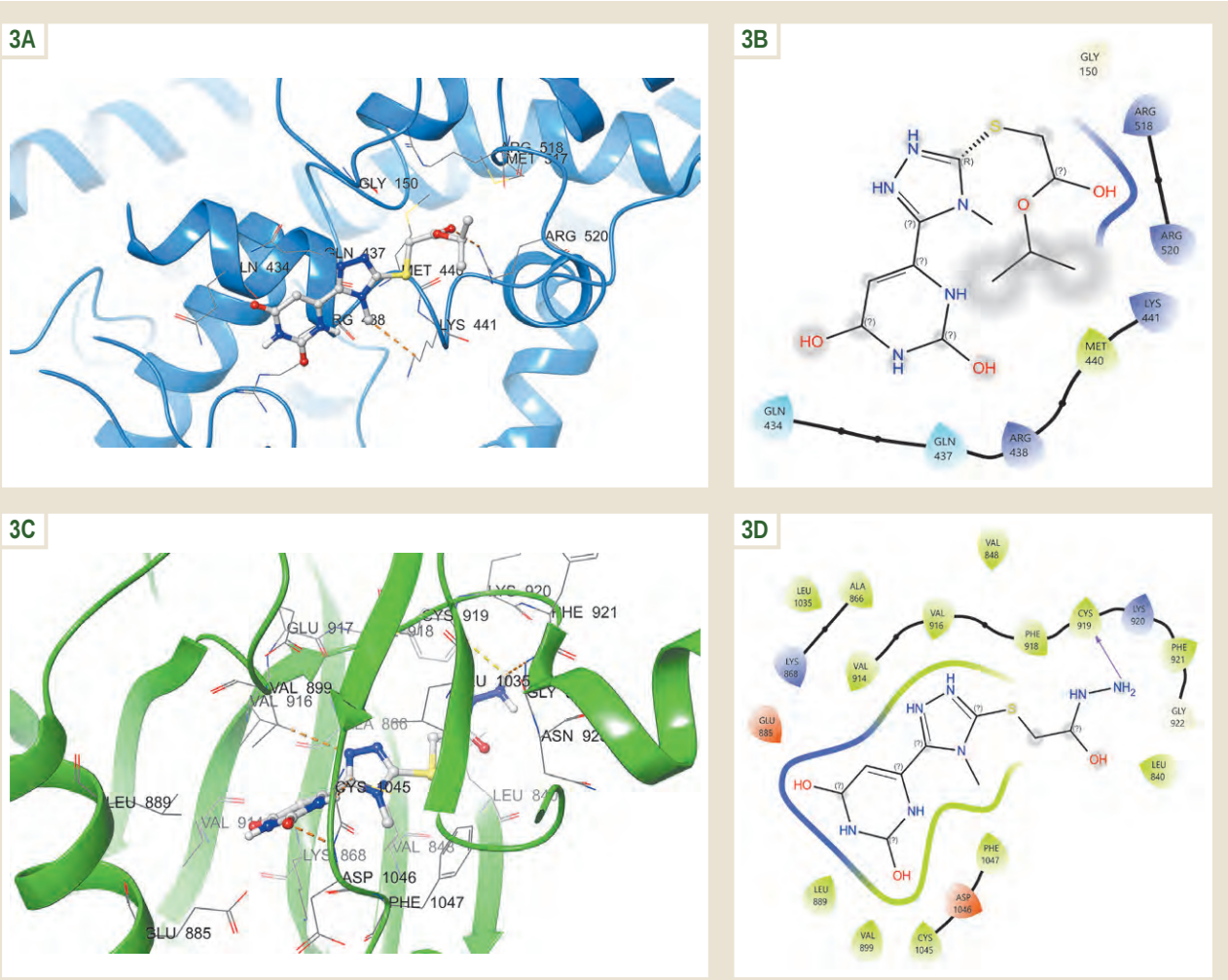


Fig. 3. Representative 3D binding poses and 2D interaction diagrams of the prioritized *N*-methyl derivatives. **A:** 3D binding pose of compound 16 in 5-LOX; **B:** corresponding 2D interaction diagram of compound 16, the top-ranked ligand for 5-LOX (-8.61 kcal/mol); **C:** 3D binding pose of compound 19 in VEGFR-2; **D:** corresponding 2D interaction diagram of compound 19, the leading overall multi-target candidate and the top-ranked ligand for VEGFR-2 (-8.48 kcal/mol).

high polarity, limited predicted gastrointestinal absorption, and mutagenicity- and carcinogenicity-related computational alerts illustrate that superior docking does not necessarily indicate superior development potential. These toxicity predictions should be regarded as screening alerts rather than evidence of experimental toxicity.

Compound **18** represented an additional target-oriented candidate, combining strong 5-LOX recognition with the most favorable MMP-2 docking score and good predicted aqueous solubility. Accordingly, compounds **16**, **18**, and **19** represent complementary profiles rather than a simple ranking: **16** provides the most balanced integrated profile, **18** is weighted toward inflammation- and remodeling-associated targets, and **19** demonstrates the broadest molecular recognition but also greater predicted pharmacokinetic and safety liabilities.

Protein–ligand interaction analysis supported different mechanisms of molecular recognition among the prioritized compounds. Both hydrophobic and hydrogen-bonding interactions contributed to stabilization within the investigated binding regions. Notably, no direct ligand coordination with the catalytic Fe ion of 5-LOX or Zn^{2+} ions of MMP-2 was detected. The favorable docking scores for these targets should therefore be interpreted primarily as noncovalent molecular recognition rather than evidence of a metal-chelation mechanism.

From a wound-healing perspective, favorable recognition of thrombin, 5-LOX, VEGFR-2, and MMP-2 should not be interpreted as evidence that simultaneous inhibition of all four proteins would be therapeutically beneficial. These targets participate in different and temporally regulated processes, including hemostasis, inflammation, angiogenesis, and extracellular-matrix remodeling. The present four-target panel therefore represents a molecular interaction map for identifying differentiated multi-target profiles rather than a proposed four-target inhibitory mechanism. Similarly, low predicted gastrointestinal absorption of the more polar compounds may be less restrictive if future development focuses on local or topical administration, although predicted safety liabilities remain relevant and require experimental assessment.

The principal limitation of this study is its computational nature. Docking scores are derived from simplified scoring functions and predominantly static protein structures and therefore cannot be interpreted as experimental binding affinities or functional activity. Likewise, SwissADME and ADMETlab outputs represent model-based predictions rather than experimentally established pharmacokinetic or toxicological properties. Consequently, the identified profiles should be considered hypothesis-generating and require biochemical, cellular, and safety validation.

Overall, **16** and **19** were selected as the principal candidates for further investigation. Compound **16** combined strong multi-target recognition with the more balanced physicochemical and predicted ADMET profile, whereas **19** showed the strongest overall docking profile but also more pronounced predicted permeability and safety limitations. Compound **18** remains a relevant secondary candidate because of its favorable combined 5-LOX/MMP-2 profile.

Conclusions

1. The *N*-methyl derivatives demonstrated distinct target-dependent molecular recognition profiles across thrombin, 5-LOX, VEGFR-2, and MMP-2, representing molecular targets associated with hemostasis, inflammation, proliferation/angiogenesis, and extracellular-matrix remodeling, respectively. Structure–property analysis revealed a clear trade-off between increasing lipophilicity, target-specific docking performance, and predicted aqueous solubility, particularly within the compounds **3**–**12** subset.

2. Integrated molecular docking identified **16**, **18**, and **19** as the principal multi-target candidates. Compound **16** showed the most favorable docking score toward 5-LOX (-8.61 kcal/mol), **18** toward MMP-2 (-8.25 kcal/mol), and **19** toward VEGFR-2 (-8.48 kcal/mol), while **19** exhibited the most favorable overall four-target docking profile (mean score -8.12 kcal/mol). Protein-ligand interaction analysis demonstrated that these profiles were supported by distinct combinations of hydrogen-bonding and hydrophobic interactions rather than by a common binding mechanism or direct metal coordination.

3. Integration of docking with SwissADME and ADMETlab predictions demonstrated that docking affinity alone was insufficient for lead prioritization. Compound **16** displayed a comparatively balanced overall computational profile, **18** combined strong 5-LOX/MMP-2 recognition with favorable predicted solubility, whereas **19** showed the broadest multi-target docking profile but also presented permeability-related limitations and computational safety alerts. These three compounds therefore represent complementary candidates for subsequent experimental validation of their target-specific activities and wound-healing-related potential.

Prospects for further research. Further studies should focus on experimental validation of the prioritized compounds using target-specific biochemical assays for thrombin, 5-LOX, VEGFR-2, and MMP-2, followed by evaluation of cytocompatibility, wound-healing-related cellular responses, and topical delivery properties. Particular attention should be given to experimentally verifying the pharmacokinetic and safety liabilities identified by the computational ADMET analysis.

AI statement

OpenAI ChatGPT (GPT-5.6 Sol, OpenAI, 2026) was used solely for language editing to improve the grammar, clarity, and readability of the manuscript. The authors reviewed and approved all edited text and take full responsibility for the content of the final manuscript.

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Conflict of interest

Yuriy Karpenko is a member of the Editorial Team of *Current issues in pharmacy and medicine: science and practice* but was not involved in the peer review process or the decision to publish this article and had no access to information about the identities of the reviewers. The manuscript was handled by an independent handling editor. The authors declared no other potential conflicts of interest.

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