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Section 1. Preventive medicine

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DISCOVERY OF SMALL MOLECULE INHIBITORS OF MAO-B FOR ALZHEIMER'S DISEASE USING PHARMACOPHORE-BASED VIRTUAL SCREENING

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Abstract

Effective therapies are needed to mitigate Alzheimer's disease (AD), a neurodegenerative dementia that harms cognitive function in over 10% of people older than 65. Although monoamine oxidase B (MAO-B) is a critical therapeutic target for AD, only three MAO-B inhibitors (rasagiline, selegiline, and safinamide) are currently approved, and they are mainly used for treating Parkinson's Disease. To identify novel MAO-B inhibitors as treatments for AD, *in silico* drug discovery was employed as a cost-effective and efficient approach for screening a vast chemical space. Geometric, energetic, and machine learning methods were used to evaluate potential binding sites, which were subsequently assessed with molecular docking for 20 potential MAO-B inhibitors identified from pharmacophore mapping. These 20 molecules were then analyzed for their pharmacokinetic and toxicological properties via ADMET prediction, and Z56776036 and Z1980993192 were selected as the two most promising drug candidates. These lead compounds had high binding affinity (docking scores below –9 kcal/mol), strong ADME profiles, and low toxicity (LD50 values above 1000 mg/kg). This experiment proposes an innovative method of MAO-B inhibitor discovery. It represents a promising starting point for future work focused on further testing of the 2 lead compounds through *in vitro* screening and additional *in silico* discovery of lead compounds using the methodology of this project.

Keywords: *Alzheimer's disease, monoamine oxidase B, pharmacophore mapping, molecular docking, ADMET prediction, drug discovery*

Introduction

Alzheimer's disease (AD), a type of neurodegenerative dementia, impacts memory and cognitive abilities in over 57 million people worldwide alongside other dementias (*The Lancet*, 2022). It is estimated that 1 in 9 people over the age of 65 have Alzheimer's, and researchers predict that over 152 million people worldwide will have dementia by 2050 (*The Lancet*, 2022; Alzheimer's Associ-

ation, 2024). Additionally, healthcare costs for AD patients are projected to reach almost $1 trillion in 2050 (Alzheimer's Association, 2024). Therefore, treating AD remains a significant concern both for public health and economic stability.

Current FDA-approved drugs for AD include acetylcholinesterase inhibitors (AChEIs), NMDA receptor antagonists, and monoclonal antibodies targeting Aβ proteins (Zhang et al., 2024). AChEIs, such as donepezil, galantamine, and rivastigmine, are the main type of pharmacological treatment for AD (Zuliani et al., 2024). Although they mildly mitigate cognitive decline, AChEIs remain mostly symptomatic (Zuliani et al., 2024). Memantine, the only NMDA receptor antagonist currently approved for AD treatment, is prescribed for patients with moderate to severe AD (Balázs et al., 2021). Usually a second-line treatment after AChEIs, memantine has a small benefit in moderate to severe AD, but not in mild AD (Balázs et al., 2021). Finally, newer drugs for Aβ proteins include aducanumab, lecanemab, and donanemab (Ebell et al., 2024). Cognitive benefits are statistically significant but small, and risks such as edema or hemorrhage remain prevalent with these drugs (Ebell et al., 2024). As a result, many monoclonal antibodies for AD have been discontinued due to their side effects. Since current AD treatments have many drawbacks, researchers have been exploring more promising pathways for AD to develop new drugs.

Two main pathways for AD are the amyloid-β (Aβ) pathway and the neuroinflammation pathway, which have gained more attention in recent years over older pathways such as the cholinergic hypothesis. The amyloidogenic pathway occurs when β-secretase cleaves the amyloid precursor protein (APP) instead of α-secretase, forming soluble APP-β and a C-terminal fragment (CTFβ) instead of soluble APP-α (Hampel et al., 2021). As a result, Aβ peptides are produced, and they clump together in extracellular Aβ plaques that cause aberrant signaling between neurons (Hampel et al., 2021). Additionally, the amyloidogenic pathway can lead to tau hyperphosphorylation, which causes neurofibrillary tangles that are correlated with cognitive decline (Hampel et al., 2021). The neuroinflammation pathway involves the activation of microglia and astrocytes, which lead to inflammatory signaling with neurotoxic effects (Liew et al., 2023). Positive feedback loops as well as Aβ or tau buildup contribute to neuroinflammation, either through further glial activation or increased Aβ accumulation via RIPK1 kinase (Liew et al., 2023; Doig, 2018).

Monoamine oxidase B (MAO-B) can offer insights into new AD treatment through the Aβ and neuroinflammation pathways. MAO-B is an enzyme that breaks down monoamine neurotransmitters such as serotonin, dopamine, and norepinephrine, which regulate mood, cognition, and behavior (Behl et al., 2021). MAO-B works by removing the amino group of the neurotransmitter and oxidizing it, producing an inactive metabolite, an aldehyde (R-CHO), ammonia (NH_3), and hydrogen peroxide (H_2O_2) as a byproduct (Behl et al., 2021). Normally, MAO-B controls mood and motor activity, acting as a metabolic barricade against amines. However, the overexpression of MAO-B enzymes can lead to oxidative stress due to H_2O_2 buildup, causing Aβ plaques and neurofibrillary tangles (Behl et al., 2021). High levels of MAO-B, which breaks down non-hydroxylated amines, are found in astrocytes surrounding Aβ plaques (Behl et al., 2021). The oxidative stress caused by MAO-B overactivity may lead to the Aβ and tau pathways by triggering neuroinflammation, potentially causing Aβ plaques or neurofibrillary tangles.

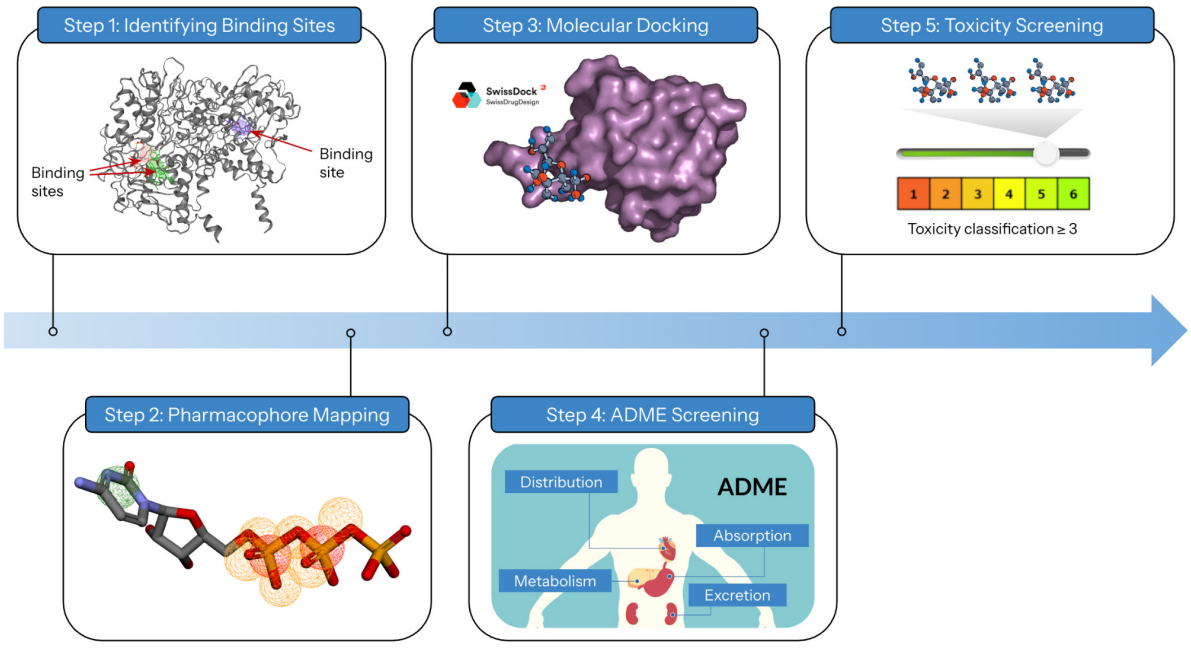
Because MAO-B is linked to two key pathways for Alzheimer's disease, monoamine oxidase inhibitors (MAOIs), an early class of antidepressants, are being explored as a promising new form of AD treatment. In Alzheimer's disease, the glutamate-GABA balance is disrupted, causing oxidative stress, and MAOIs can restore that balance by increasing GABA levels (Behl et al., 2021). MAOIs also sequester aldehydes and inhibit primary amine oxidase (PrAO), an enzyme that also produces aldehydes promoting Aβ plaque formation (Behl et al., 2021). These mechanisms indicate that MAOIs may be able to reduce oxidative stress in the brain, making them a powerful candidate for early AD treatment.

Researchers have explored various methods for developing MAOI-based AD treatment.

A study by Da Costa et al. used *in silico* preclinical screening to identify 4 lead compounds as potential MAO-B inhibitors, although these compounds have yet to undergo further testing (2024). Additionally, some propargylamines, such as selegiline and rasagiline, can be used as irreversible MAO-B inhibitors by binding covalently to the coenzyme flavin adenine dinucleotide (FAD), permanently disabling MAO-B (Chatzipieris et al., 2024). Newer compounds with internal alkynes are being explored as a way to avoid unwanted side effects of irreversible inhibition, such as upregulation of the GABA-synthesizing enzyme diamine oxidase (DAO) (Chatzipieris et al., 2024). Park et al. developed KDS2010 in 2019, a MAO-B inhibitor that is both reversible and highly selective (2019). By testing on APP/PS1 mice, the researchers discovered that KDS2010 reduces astrocytic GABA levels, bypassing the challenges of selegiline increasing DAO activity (Park et al., 2019). Beyond inhibitors for MAO-B alone, studies have also developed potential AD treatments involving drugs aimed at more than one target. Through *in silico* and *in vitro* analysis, Svobodova et al. tested 24 N-methylpropargylamino-quinazoline derivatives as multi-target directed ligands (MTDLs) for cholinesterases, monoamine oxidases, and N-methyl-D-aspartate receptors (NMDARs) in AD (2023). However, MTDLs face the challenge of selectivity, as they are designed to inhibit more than one enzyme. The potential of MAO-B inhibitors still remains largely unexplored, and no MAO-B inhibitors have passed clinical trials as of 2025. This research aims to improve upon existing work for MAO-B inhibitor discovery and focus on systematic pharmacophore-based *in silico* screening, which is cost-effective and offers rapid results.

Methodology

Figure 1. *Overview of methodology with 5 main steps*



MAO-B Binding Sites

To detect potential binding sites on the MAO-B protein that are both geometrically and energetically viable, computational tools such as DoGSiteScorer, FTSite, and P2Rank were used. DoGSiteScorer detects binding pockets, identifies their geometric and physicochemical properties, and predicts protein druggability to assign a drug score using a support vector machine (Volkamer et al., 2012). MAO-B's PDB code, 6FWC, was applied for DoGSiteScorer on https://proteins.plus/ with default settings (Reis et al., 2018). The "DoGSiteScorer" tab was selected on the website, and all settings were left as default. FTSite uses molecular probes to determine energetically favorable binding sites, as locations where the probes bind are more likely

to be optimal binding sites for ligands (Ngan et al., 2011). Code 6FWC was used on FTSite (https://ftsite.bu.edu/) with default settings. P2Rank uses machine learning to classify Solvent Accessible Surface points, which are regularly spaced points that encode geometric and physicochemical properties (Krivák & Hoksza, 2018). Code 6FWC was inputted on P2Rank with default settings on PrankWeb (https://prankweb.cz/) (Jendele et al., 2019).

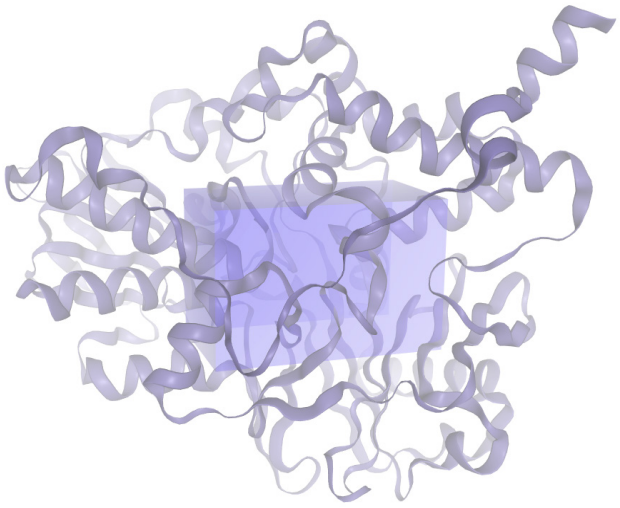
Pharmacophore Mapping

Pharmit (https://pharmit.csb.pitt.edu/) was used to generate a pharmacophore map and virtually screen small molecules to match the map (Sunseri & Koes, 2016). Pharmit filters through large drug databases and ranks results via energy minimization (Sunseri & Koes, 2016). To perform virtual screening with pharmacophore mapping in Pharmit, PDB code 6FWC was entered, "FAD" was selected from the adjacent dropdown menu, binding site waters were ignored, and the Enamine database was used. Pharmacophoric features of MAO-B were selected in areas likely to be optimal binding sites, creating 3 maps that captured different areas of the MAO-B enzyme (see Figure 8). Pharmit scanned the Enamine database and produced a list of molecules that matched the pharmacophore maps, from which 20 molecules were selected that had the least root mean square deviation.

Molecular Docking

After identifying the 20 top compounds from the Enamine database, molecular docking with SwissDock was used to test the ability of these compounds to dock on MAO-B (Grosdidier et al., 2011; Bugnon et al., 2024). On swissdock.ch, docking with attractive cavities was used with the SMILES code from Enamine (enaminestore.com) as the ligand and code 6FWC as the target. Chain B of the MAO-B enzyme was selected, and none of the heteroatoms were kept. Chain B was chosen because FTSite detected more potential binding sites on Chain B than Chain A. The search space was then defined with box center (20Å, 128Å, 18Å) and box size (15Å, 17Å, 27Å), as shown in Figure 2. The process was repeated for all 20 compounds.

Figure 2. *Setup of the SwissDock molecular docking. The purple ribbon represents chain B of the MAO-B protein, while the box represents the area where docking was simulated*



ADME Screening

Based on the results of the molecular docking, the top 10 drug candidates were chosen by most negative SwissParam score. SwissADME was used to determine various physicochemical features for the 10 compounds, as it identified their absorption, distribution, metabolism, and excretion (ADME) capabilities in the human body (Daina et al., 2017). To perform screening with SwissADME, the SMILES code obtained from the Enamine database was entered at http://www.swissadme.ch/. The molecular weight, number of hydrogen bond acceptors, number of hy-

drogen bond donors, and consensus LogP value was used for each drug candidate to determine whether the compound satisfied Lipinski's Rule of Five. Finally, the water solubility (Insoluble < Poorly < Moderately < Soluble < Very < Highly), gastrointestinal (GI) absorption classification, and blood-brain barrier (BBB) permeability were evaluated for each compound. For the screening, the consensus LogP value was used instead of the iLogP value, because the iLogP value was often an outlier from the other calculated LogP values. The ESOL Log S value was used for water solubility. Through this analysis, the number of drug candidates was narrowed down from 10 to 7.

Toxicity Screening

After the ADME screening, toxicity screening was performed on the 7 remaining compounds using ProTox 3.0 (https://tox.charite.de/protox3/). Tox Prediction was selected and the SMILES from the Enamine database was pasted in. All fields in the model prediction box were checked before starting the prediction. Only compounds that had an LD50 value greater than 400 mg/kg and a toxicity classification above 3 were kept, which narrowed the number of compounds down from 7 to 3. Then, examining the network and toxicity radar charts determined the final 2 safest potential candidates.

Results and Discussion

MAO-B Binding Sites

In order to determine potential drug candidates, binding sites on the protein that drugs could bond to were detected. A geometric method (DoGSiteScorer), an energetic method (FTSite), and a machine learning method (P2Rank) were used to predict potential binding sites on the MAO-B protein. DoGSiteScorer, the geometric method, was able to detect 38 potential binding sites. Table 1 shows all of the sites that had a drug score ≥ 0.5, of which there were 17. Two sites, P_0 and P_1, were noticeably larger than the others, although a smaller site (P_5) was ranked first by drug score.

Table 1. *The top 17 binding sites detected by DoGSiteScorer that had drug score ≥ 0.5, sorted by drug score*

Name	Volume (Å³)	Surface Area (Å²)	Drug Score
P_5	411.14	396.08	0.87
P_0	2077.85	1722.15	0.81
P_1	2042.91	1725.6	0.81
P_2	553.72	721.08	0.81
P_3	548.35	748.07	0.79
P_4	460.78	845.28	0.74
P_9	298.12	385.62	0.73
P_11	293.54	173.93	0.72
P_6	370.36	672.77	0.67
P_7	308.87	381.52	0.67
P_10	294.01	326.82	0.65
P_8	306.82	585.96	0.63
P_14	269.67	420.62	0.56
P_12	290.38	514.82	0.54
P_13	277.1	520.46	0.51
P_15	260.66	345.48	0.51
P_20	162.97	247.66	0.5

As seen in Figures 3 and 4, P_0 (yellow) and P_1 (purple) are much larger than the other binding sites. Figure 3 shows the top 3 binding sites, including P_0 and P_1 as well as P_5, which is much smaller but has the highest drug score assigned by DoGSiteScorer. Figure 4 shows all 17 potential binding sites.

Figure 3. *Top 3 binding sites identified by DoGSiteScorer. The red and blue ribbons represent the protein structure, while the green, yellow, and purple represent the binding sites (P_5, P_0, and P_1 respectively)*

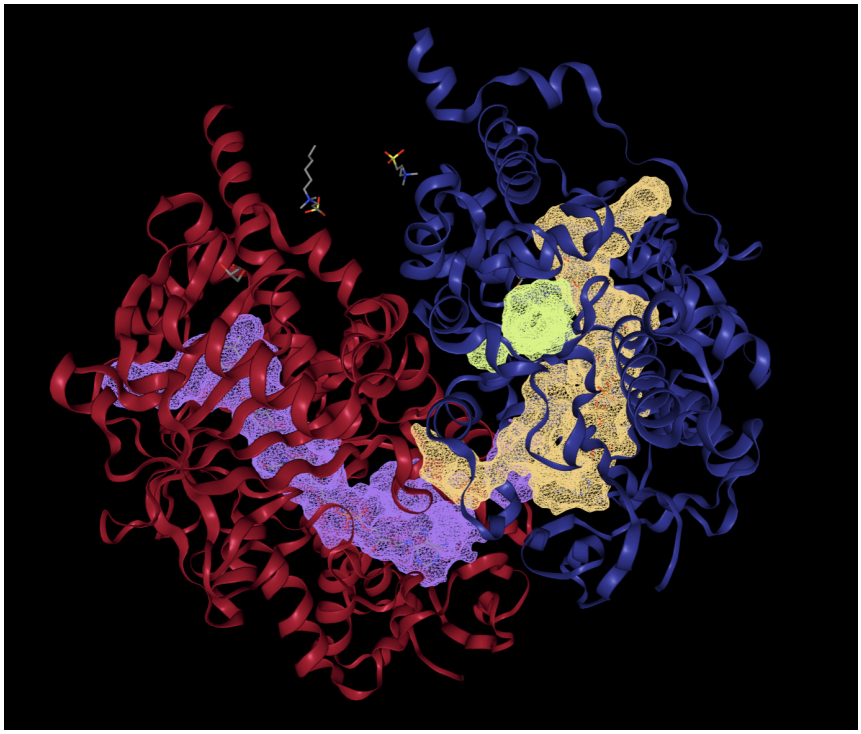
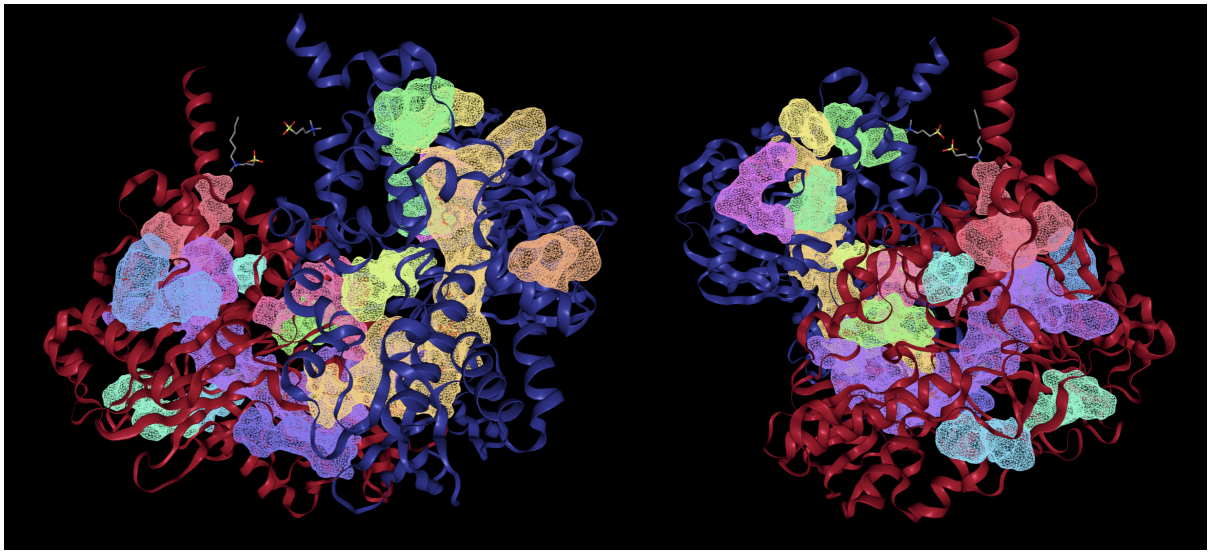
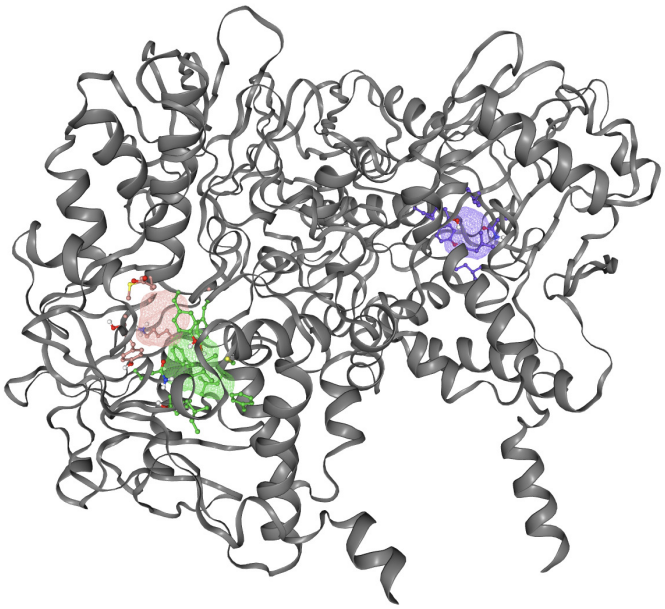


Figure 4. *All 17 potential binding sites identified by DoGSiteScorer, shown on the protein from two different angles*



The energetic method, FTSite, was able to detect 3 possible binding sites, as shown in Figure 5. Two sites were on the side colored blue on DoGSiteScorer, and one site was on the side colored red (see above). Since FTSite is based on energetic rather than geometric favorability, it identified less potential binding sites.

Figure 5. *Results of the FTSite energetic binding site prediction for the MAO-B protein. The gray ribbon represents the protein structure, while the green, red, and purple represent potential binding sites.*



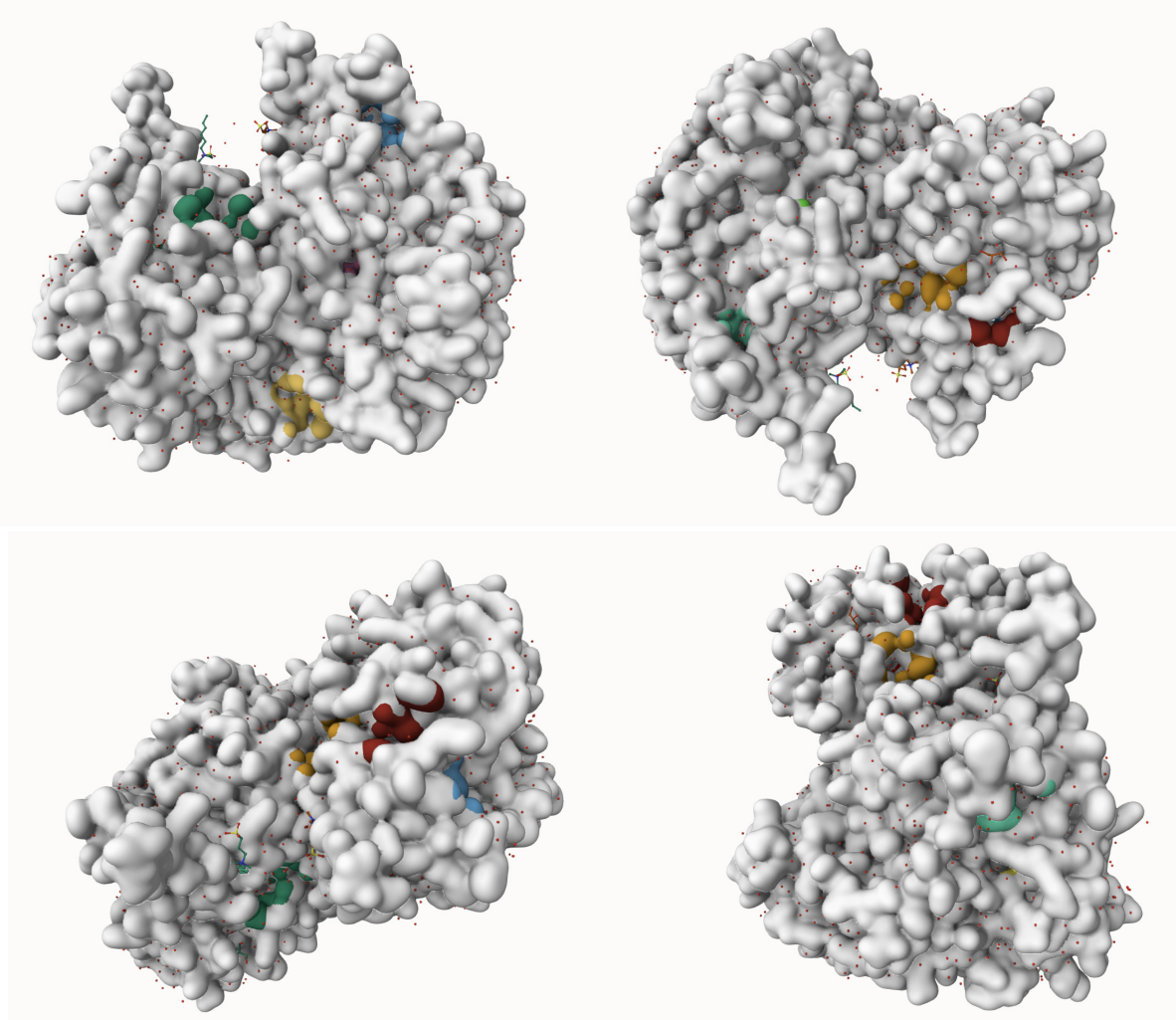
Finally, the machine learning method, P2Rank, was able to detect 12 binding sites, as shown in Table 2. Sites were ranked by score, and the data also included the number of residues for each site. The top two binding sites were consistent with DoGSiteScorer, as they were much larger than the rest. On PrankWeb, these two sites also had significantly higher scores and larger numbers of residues.

Table 2. *12 potential binding sites for the MAO-B protein detected by P2Rank, sorted by score.*

Rank sorted ascending	Score	# of residues
1	51.19	56
2	45.43	50
3	3.87	14
4	3.62	15
5	3.34	14
6	3.24	7
7	2.70	13
8	2.49	11
9	2.39	14
10	1.95	8
11	1.35	5
12	1.04	13

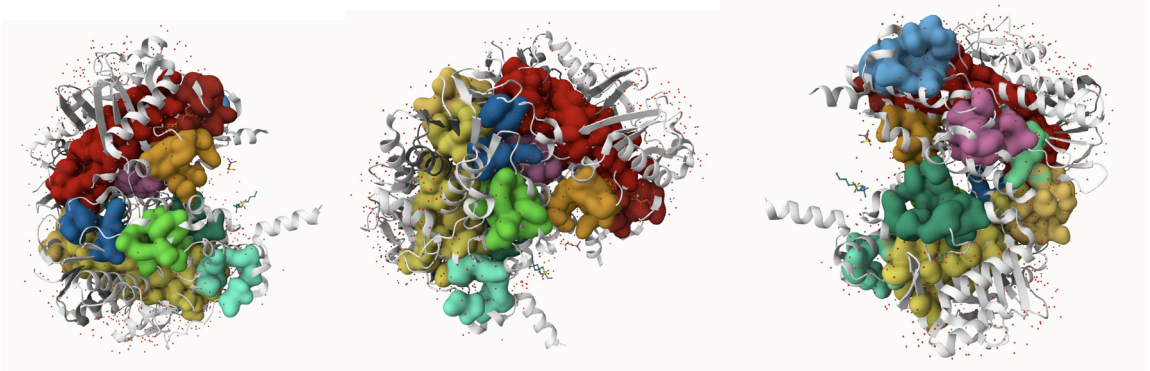
Figures 6 and 7 show various binding sites colored on the protein. Figure 6 shows the binding sites on the surface, and figure 7 shows them inside the MAO-B enzyme. As seen in figure 6, binding sites tended to be in concave pockets on the surface.

Figure 6. *Results of the P2Rank binding site prediction for the MAO-B protein. The gray represents the protein structure, while the colors represent potential binding sites. The protein is visualized by "surface" and the pockets are visualized by "surface (atoms)," shown from four different angles*



As shown in figure 7, the light yellow and red binding sites are significantly larger than the rest, suggesting that they might correspond to the sites P_0 and P_1 identified by DoGSiteScorer. These two sites also had distinctively higher scores of 51.19 and 45.43, compared with the rest of the sites with scores between 1 to 4.

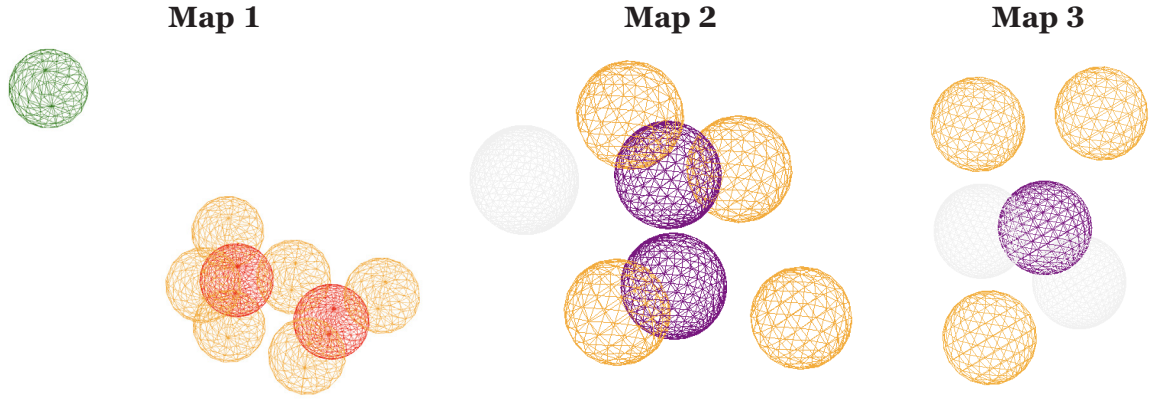
Figure 7. Results of the P2Rank binding site prediction with the protein visualized by "cartoon" and the pockets visualized by "surface (residues)," shown from three different angles



Pharmacophore Mapping

After potential binding sites were found, a pharmacophore map for the MAO-B protein that showed key features for binding was created. Instead of using the complete pharmacophore map for MAO-B, different combinations of pharmacophoric features were selected from Pharmit to create three maps with 6 to 9 features each, as shown in Figure 8. Each map focused on a distinctive aspect of MAO-B's pharmacophoric structure. The screening of the Enamine database for the first map only resulted in 3 potential drug candidates, so the second and third maps were added to find more compounds, producing 12 and 5 candidates respectively.

Figure 8. *Pharmit pharmacophore maps (1, 2, and 3 from left to right) generated from the MAO-B protein used to run virtual screening. Green spheres represent hydrophobic interactions, dark orange spheres represent negative ions, light orange spheres represent hydrogen acceptors, purple spheres represent aromatic interactions, and white spheres represent hydrogen donors*



Tables 3–5, which summarize the 20 compounds identified from the pharmacophore mapping experiment, show that the features of the compounds align closely with those of the pharmacophore maps. A lower RMSD is better, as it means the compound deviates less from the map. Compounds yielded from the third pharmacophore map had the lowest RMSD scores, whereas those from the first map had the highest RMSD scores. As shown in Figure 8, Map 1 is larger and more spread out than Map 2 and Map 3. Although the compounds generated from Map 1 had higher RMSDs, they were still included to test if a larger map might lead to drugs with better docking capabilities despite having worse matches.

Table 3. *Name, root mean square deviation (RMSD), and structure of drug candidates detected by Pharmit's virtual screening of the Enamine database with the first pharmacophore map*

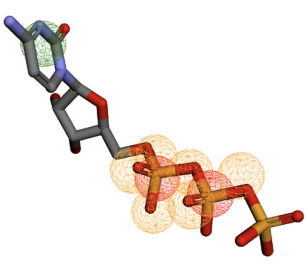
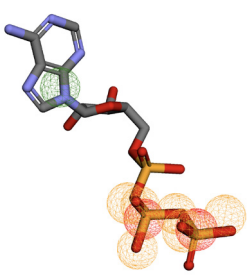
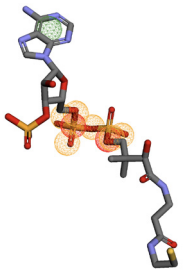
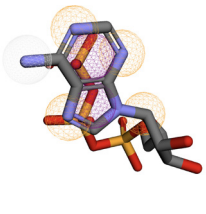
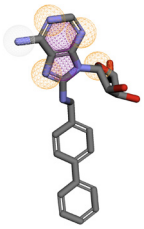
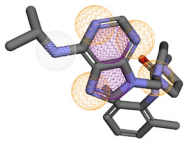
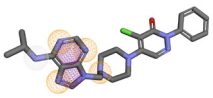
Name	Z4164535231	Z3810976496	Z3196311517
Structure			
RMSD	0.440	0.460	0.512

Table 4. *Name, root mean square deviation (RMSD), and structure of drug candidates detected by Pharmit's virtual screening of the Enamine database with the second pharmacophore map*

Name	Z3810976496	Z2065614619	Z1082764572	Z1082764448
Structure				
RMSD	0.045	0.050	0.051	0.052
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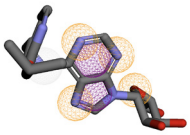
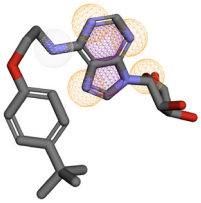
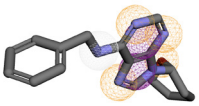
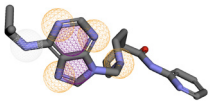
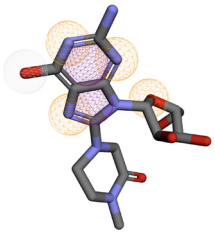
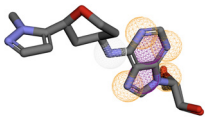
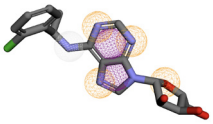
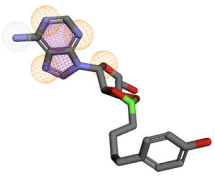
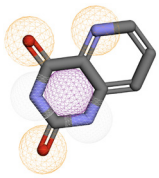
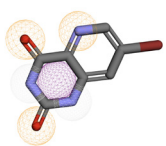
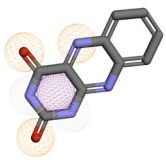
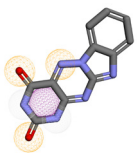
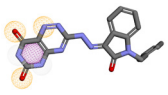
Structure				
RMSD	0.056	0.061	0.062	0.063
Name	Z7911919636	Z4122876582	Z1980908378	Z4097793914
Structure				
RMSD	0.067	0.068	0.072	0.077

Table 5. *Name, root mean square deviation (RMSD), and structure of drug candidates detected by Pharmit's virtual screening of the Enamine database with the third pharmacophore map.*

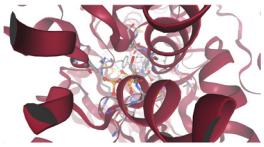
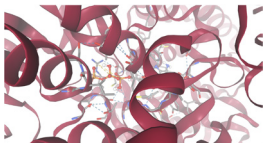
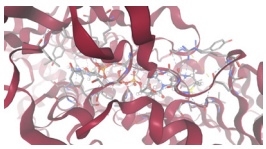
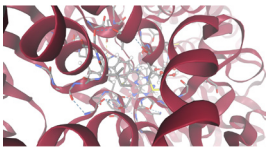
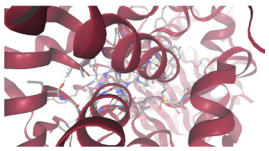
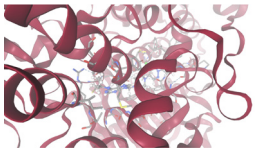
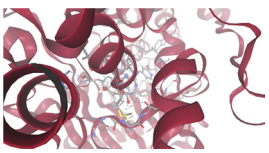
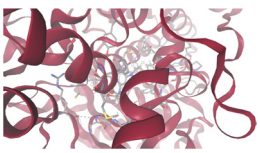
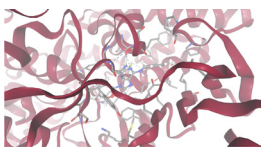
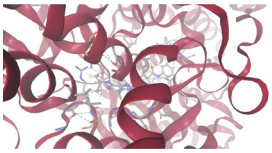
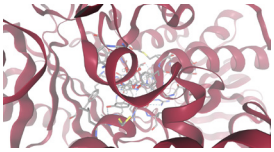
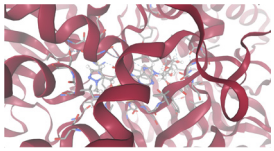
Name	Z1201626990	Z1269216848	Z56790788	Z56758453	Z56776036
Structure					
RMSD	0.027	0.027	0.027	0.028	0.029

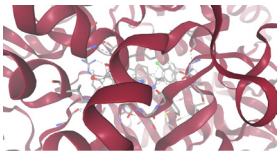
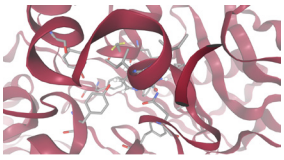
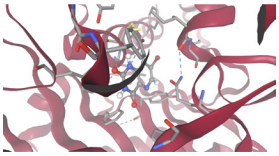
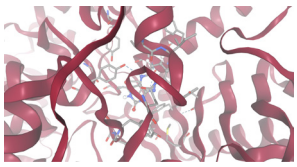
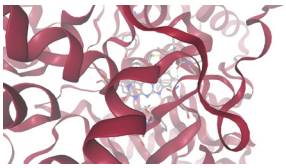
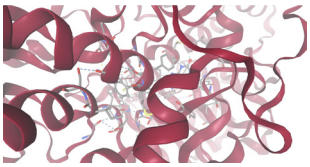
Molecular Docking

After molecular docking was assessed for each of the 20 compounds, most had a SwissParam score around –8, –9, or –10. During the docking simulation, the inhibitor was given the freedom to rotate around a defined box on the target and dock wherever possible. SwissDock then quantified the energy of

the interaction to determine how favorable binding would be. The top SwissParam score represented the Gibbs free energy (ΔG) of the best interaction in kilocalories per mole. The more negative the ΔG value, the more spontaneous the interaction, meaning that it consumed less energy and was more favorable. 10 compounds were selected by the most negative SwissParam score. The compound that performed the best was Z3196311517, followed by Z1082764448, the only two candidates that had SwissParam scores below –10. The SMILES of compound Z4097793914 was not accepted by SwissDock, likely due to the presence of boron, so it was removed from the screening. Compound Z3810976496 was found to be repeated, so its duplicate was taken out. The names and SwissParam scores of the top 10 compounds are bolded in Table 6 below. Although the three candidates identified from the first pharmacophore map had worse RMSD scores than the other seventeen, their SwissParam scores were all in the top 10 compounds for the molecular docking experiment. Compound Z3196311517 had the worst RMSD score, but it also had the most negative SwissParam score. The candidates identified from the third pharmacophore map generally had more positive SwissParam scores, likely due to their smaller size.

Table 6. *Results of molecular docking with SwissDock. In the residue interaction figures, the red ribbons represent the protein structure, the blue represents hydrogen bonds, and the yellow represents ionic interactions. The top 10 drug candidates are bolded*

Name	**Z4164535231**	**Z3810976496**	**Z3196311517**
SwissParam Score (kcal/mol)	**-9.8520**	**-9.9056**	**-10.7236**
Residue Interaction Figure			
Name	**Z2065614619**	**Z1082764572**	**Z1082764448**
SwissParam Score (kcal/mol)	**-9.4043**	**-9.7102**	**-10.6647**
Residue Interaction Figure			
Name	**Z1980993192**	**Z1980914346**	Z56780075
SwissParam Score (kcal/mol)	**-9.4726**	**-9.6217**	-8.5754
Residue Interaction Figure			
Name	**Z1082766136**	Z7911919636	Z4122876582
SwissParam Score (kcal/mol)	**-9.6193**	-8.2044	-8.9549
Residue Interaction Figure			

Name	Z1980908378	Z1201626990	Z1269216848
SwissParam Score (kcal/mol)	-8.7293	-6.4432	-6.7312
Residue Interaction Figure			
Name	**Z56790788**	**Z56758453**	**Z56776036**
SwissParam Score (kcal/mol)	-7.2137	-7.7093	**-9.7320**
Residue Interaction Figure			

ADME Screening

After performing ADME screening on the top 10 remaining drug candidates, the top 7 were selected based on whether they satisfied Lipinski's Rule of Five, a set of four rules that predict oral bioavailability (Lipinski et al., 1997). The molecular weight (MW), number of hydrogen bond (H-bond) acceptors, number of H-bond donors, and consensus LogP value for each drug candidate were used to evaluate their adherence to Lipinski's Rule of Five. Although they were all in the top 10, none of the three drug candidates selected from the first pharmacophore map satisfied Lipinski's Rule of Five, likely due to their large size. As a result, compounds Z1082764448, Z56776036, Z1082764572, Z1980914346, Z1082766136, Z1980993192, and Z2065614619 were selected as the top 7 potential MAO-B inhibitors. Out of these seven, compound Z1082764448 had the most negative SwissParam score. Table 7 summarizes the results of the ADME screening.

Table 7. *Physicochemical properties of 10 potential MAO-B inhibitors identified by SwissADME, sorted by SwissParam score. Green highlighting indicates which compounds satisfy Lipinski's Rule of Five ("RoF" column)*

Molecule	Mol. Weight	# H-bond acceptors	# H-bond donors	LogP Value	RoF	Water Solubility	GI absorption	BBB permeant
Z3196311517	767.53 g/mol	19	9	-3.20	No	Highly soluble	Low	No
Z1082764448	479.97 g/mol	6	1	2.44	Yes	Moderately soluble	High	No
Z3810976496	551.14 g/mol	16	5	-9.72	No	Highly soluble	Low	No
Z4164535231	563.15 g/mol	17	7	-9.79	No	Highly soluble	Low	No
Z56776036	414.38 g/mol	7	3	1.52	Yes	Soluble	Low	No
Z1082764572	436.55 g/mol	6	2	2.05	Yes	Moderately Soluble	High	No
Z1980914346	443.50 g/mol	8	4	1.54	Yes	Moderately Soluble	High	No

Molecule	Mol. Weight	# H-bond acceptors	# H-bond donors	LogP Value	RoF	Water Solubility	GI absorption	BBB permeant
Z1082766136	394.47 g/mol	6	2	1.59	Yes	Soluble	High	No
Z1980993192	416.43 g/mol	9	4	0.35	Yes	Soluble	Low	No
Z2065614619	448.47 g/mol	7	5	1.26	Yes	Moderately Soluble	Low	No

Toxicity Screening

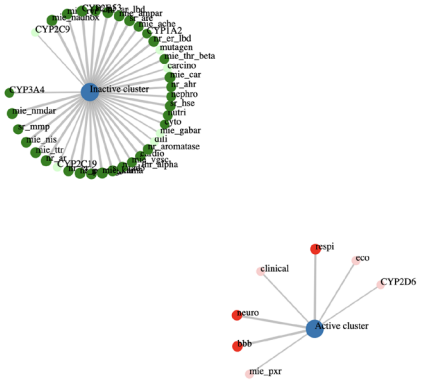
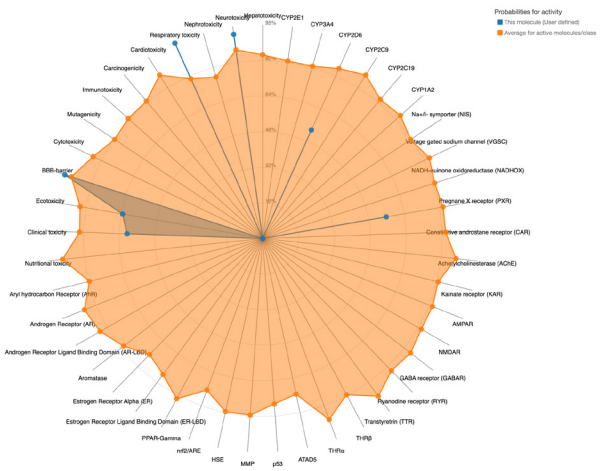
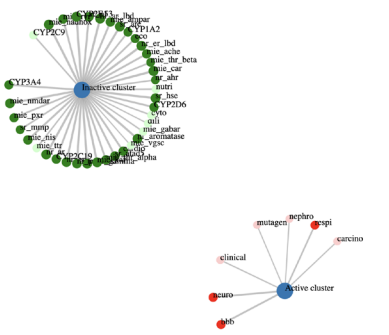
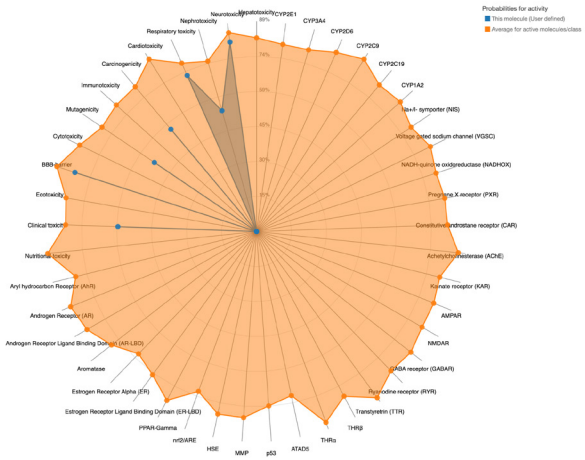
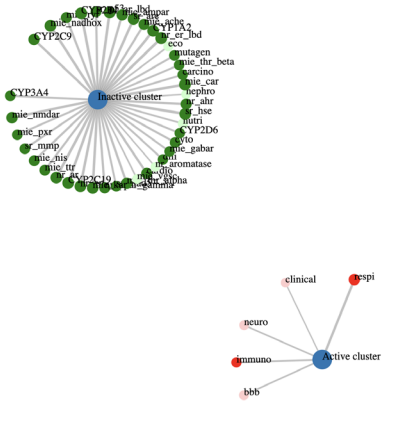
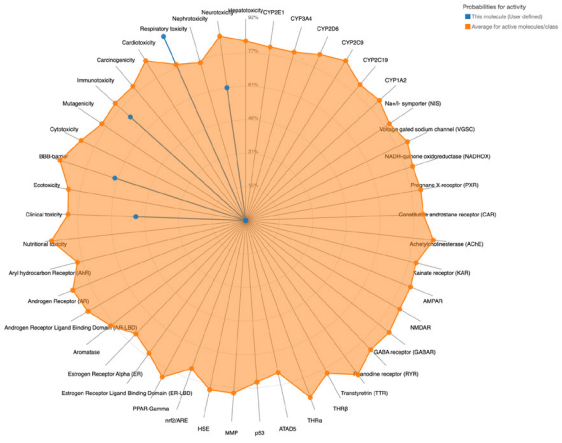
After the ADME screening, the remaining seven molecules were evaluated with ProTox-3.0 to determine their toxicity classification and LD50 value. Only compounds Z1082764448, Z56776036, and Z1980993192 were determined to be acceptably safe, as they had LD50 value above 400 mg/kg and toxicity classification above 3. The rest were deemed too toxic and eliminated from the screening. Results of the ProTox screening are shown in Table 8.

Table 8. *Toxicological properties of 7 potential MAO-B inhibitors identified by ProTox. Green highlighting indicates which compounds have both LD50 value > 400 mg/kg and toxicity classification > 3*

Name	LD50 (mg/kg)	Toxicity Classification
Z1082764448	2520	5
Z56776036	3000	5
Z1082764572	175	3
Z1980914346	29	2
Z1082766136	175	3
Z1980993192	1000	4
Z2065614619	13	2

For the remaining 3 drug candidates, the network chart and toxicity radar chart were assessed for additional toxicological analysis. The network chart shows the active (toxic) and inactive clusters, while the toxicity radar chart compares the active elements of the compound against their acceptable limits. Compounds passed the screening if they had at most one element exceeding average toxicity. Compound Z1082764448 exceeded the average toxicity for three elements (BBB by 3%, respiratory toxicity by 17%, and neurotoxicity by 7%), and compound Z1980993192 exceeded the average toxicity for one element (respiratory toxicity by 14%). As a result, only compounds Z56776036 and Z1980993192 passed the toxicity screening, although Z1980993192 has the limitation of its respiratory toxicity. Z56776036 is considered to be the safest of the top two molecules. Table 9 shows the network and toxicity radar chart results.

Table 9. *Network charts and toxicity radar charts generated by ProTox. The blue dots represent the toxicity of the compound for a specific element, while the orange dots represent the average toxicity of FDA approved drugs for that element*

Name	Network Chart	Toxicity Radar Chart
Z108...		
Z567...		
Z198...		

Conclusion

MAO-B is a critical therapeutic target for the neurodegenerative dementia Alzheimer's disease, as it causes Aβ plaques and neurofibrillary tangles, two key pathways to AD. This experiment focused on identifying novel MAO-B inhibitors with *in silico* screening to optimize for high binding affinity, druglike pharmacological properties, and low toxicity. Using computational methodology, po-

tential binding sites were identified on the MAO-B protein with DoGSiteScorer, FTSite, and PrankWeb. DoGSiteScorer was able to identify 38 binding sites, FTSite identified 3, and PrankWeb identified 12. Pharmacophore mapping was then used to screen the Enamine database, yielding 20 potential drug candidates. The 20 candidates were subsequently evaluated via molecular docking, and 10 were determined to be bioactive. SwissADME then identified that 7 of the top 10 adhered to Lipinski's Rule of Five. Finally, for toxicity prediction, ProTox was used to identify the 2 lead compounds with toxicity classification above 3 and at most one active element exceeding average toxicity. This experiment successfully discovered two promising MAO-B inhibitors as treatment for Alzheimer's disease. The final candidates, Z56776036 and Z1980993192, had excellent docking scores of –9.7320 and –9.4726 respectively, strong ADME profiles, and high LD50 values of 3000 mg/kg and 1000 mg/kg respectively. This study represents a valuable starting point for future work involving additional pharmacophoric screening targeting different areas of the MAO-B protein, as well as molecular docking for Chain A of the MAO-B enzyme with SwissDock. Further testing of the 2 lead compounds through *in vitro* or *in vivo* screening is needed to confirm this paper's findings, and additional *in silico* discovery of lead compounds can be conducted using the effective, low-cost methodology described in this paper.

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STATISTICAL MODELING OF INTERMITTENT AMLODIPINE DOSING USING MONTE CARLO SIMULATION AND REAL-WORLD BLOOD PRESSURE DATA

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Abstract

Hypertension affects over 1.28 billion adults worldwide, yet treatment adherence remains low. Amlodipine, a calcium channel blocker with a long half-life, is commonly prescribed once daily, but many patients self-modify their dosing schedules. This study evaluated the effect of intermittent amlodipine dosing on blood pressure (BP) control using real-world data and Monte Carlo simulation. Blood pressure readings were collected over three months from a patient on varying dosing regimens (once daily [QD], once every other day [QOD], once every 2 days [Q2D], once weekly [Q7D], and once every 10 days [Q10D]). Statistical comparison showed no significant difference in systolic or diastolic blood pressure among dosing regimens. Monte Carlo simulations (N=1000) revealed normally distributed systolic BP values with overlapping distributions across dosing schedules. Predicted proportions of systolic BP exceeding 120 mmHg ranged from 12.2% to 27.2%, while SBP >140 mmHg occurred only twice across all regimens. Coefficient of variation for SBP was <10% in all scenarios. Findings suggest intermittent dosing has limited impact on BP control due to amlodipine's long half-life, supporting flexibility in individualized dosing schedules.

Keywords: *hypertension; amlodipine; intermittent dosing; blood pressure variability; real-world data; Monte Carlo simulation*

Introduction

Hypertension is a major global health burden, affecting an estimated 1.28 billion adults aged 30–79 years, with two-thirds residing in low- and middle-income countries (WHO, 2025). In the United States, nearly half of adults have hypertension, yet only 21% achieve adequate control. Medication adherence remains a major challenge; real-world studies report that fewer than 55% of patients adhere to prescribed antihypertensive regimens (Wogen et al., 2003).

Amlodipine, a dihydropyridine calcium channel blocker, is widely prescribed due to its long elimination half-life (30–50 hours) and sustained antihypertensive effect. The recommended dose ranges from 5 to 10 mg once daily (Wang et al., 2023). However, patients frequently self-adjust their dosing schedules, raising concerns about efficacy

and safety. While amlodipine's pharmacokinetics suggest tolerance to missed doses, systematic evaluations of intermittent dosing schedules remain scarce.

This case study investigates the impact of varying amlodipine dosing frequencies on blood pressure control using real-world data and Monte Carlo simulation. The study aims to determine whether alternative dosing schedules maintain therapeutic effectiveness and support a personalized medicine approach.

Methods

Data Collection

Blood pressure data were collected prospectively over three months from one patient receiving amlodipine 5 mg. The patient followed several dosing regimens: once daily (QD), once every other day (QOD), every 2 days (Q2D), weekly (Q7D), and every 10 days (Q10D).

Measurements were taken using a calibrated home BP monitor (Microlife®). For each assessment, at least three readings were obtained at 3-minute intervals in the morning after 15 minutes of seated rest. Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded.

Data Analysis

Observed BP values were averaged per dosing schedule. Comparisons between regimens were conducted using ANOVA. Monte Carlo simulations (N=1000 iterations) were employed to predict distributions of SBP under each dosing schedule, incorporating variability. Primary endpoints included:

- Proportion of SBP readings <120 mmHg and <140 mmHg.
- Variability of SBP (coefficient of variation, CV%).

Results

Observed Data

Comparison of the actual BP data across various treatment schedules did not reveal a statistically significant difference (ANOVA p-value >0.05) in SBP and DBP despite small fluctuations were observed among various dosing schedules (Figure 1 and Figure 2).

Figure 1. *Measured SBP (Orange) and DBP (Yellow) Readings over Time and their Moving Averages*

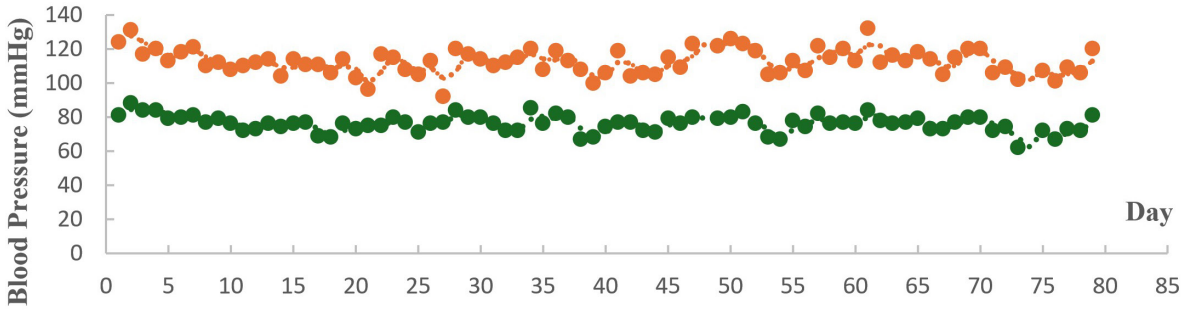
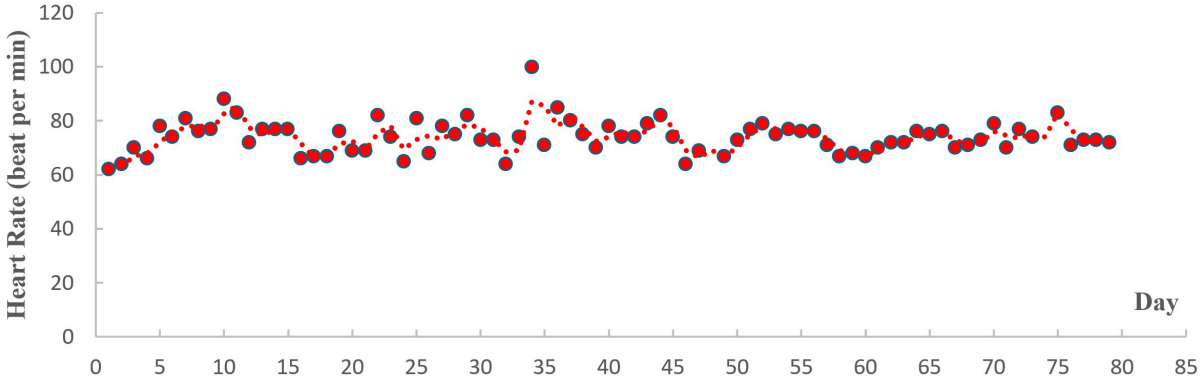


Figure 2. *Measured HR (Red) Readings over Time and their Moving Averages (Dotted Lines)*



Monte Carlo Simulation

Monte Carlo simulations (N = 1000 times) indicated that SBP data had a normal distribution with a central tendency (Figure 3) and overlapping of data distribution among various dosing schedules (Figure 4).

Monte Carlo simulations also showed that the proportion above SBP target (120 mmHg based on the American Heart Association guideline) was comparable, ranging from 12.2% to 27.2% given the inherent variability in BP (Table 1).

There were only two predicted episodes of SBP exceeding 140 mmHg across all dosing schedules.

Descriptive statistics of Monte Carlo simulation results indicated that the SBP data variability was generally less than 10% for all treatment schedules (coefficient of variation [CV]% = 5.1 to 7.0%) (Table 2).

Figure 3. *Distribution of Predicted SBP Values Using Monte Carlo Simulation for various Dosing Schedules*

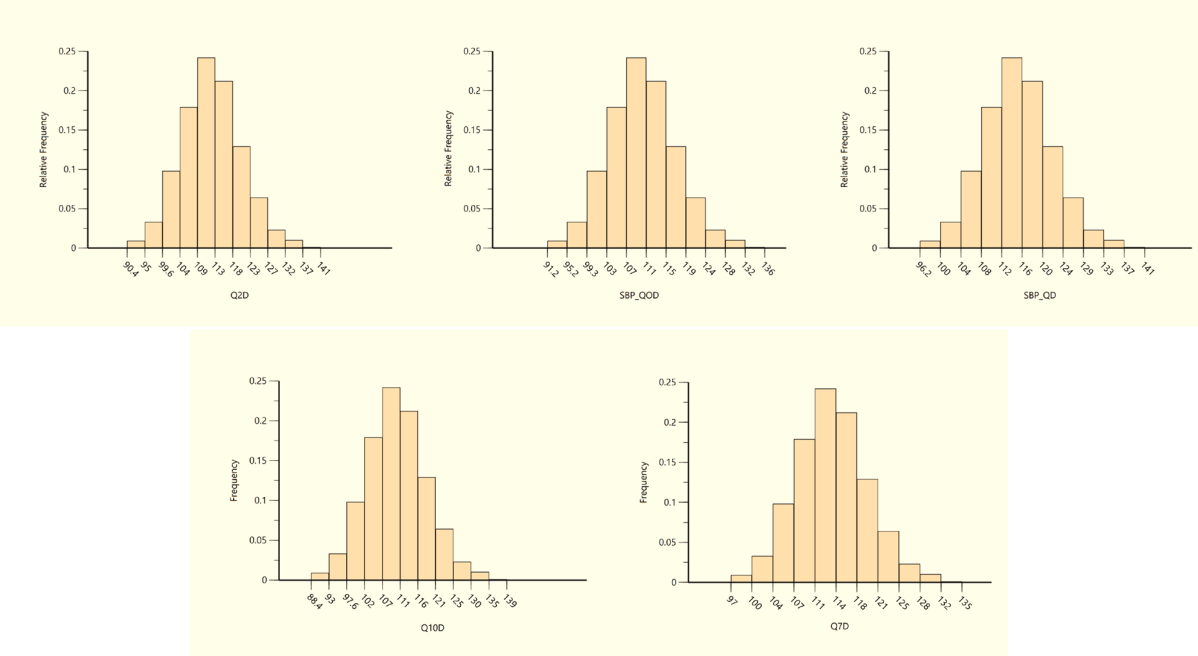


Figure 4. *Box Plots of Predicted SBP Values Using Monte Carlo Simulation for various Dosing Schedules*

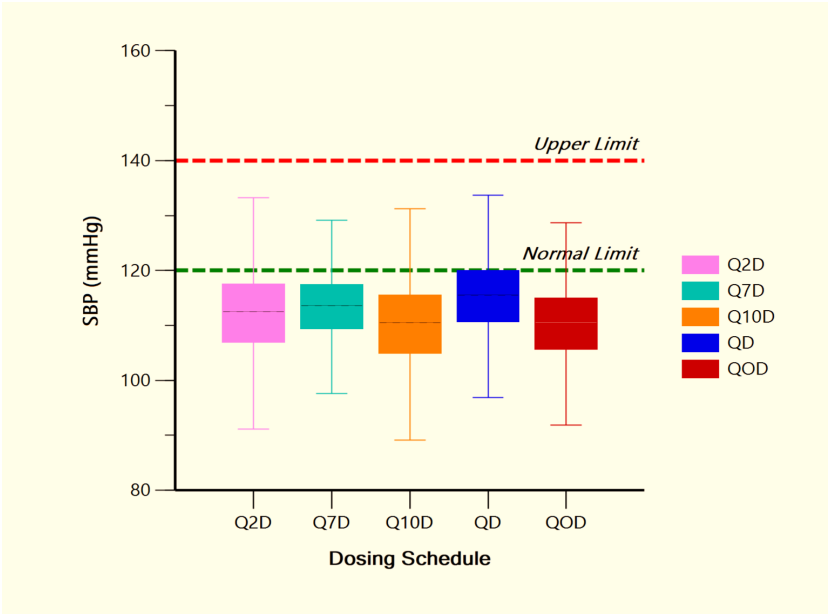


Table 1. *Percentage of Predicted SBP Values for various Dosing Schedules that are over Cutoffs*

% of simulations	QD	QOD	Q2D	Q7D	Q10D
≥ 120 mmHg	27.2	9.8	18.2	15.7	12.2
≥ 140 mmHg	0.01	0	0.01	0	0

Table 2. *Descriptive Statistics of Predicted SBP for various Dosing Schedules Based on Monte Carlo Simulation*

Variable	Dosing Schedule	N	Mean	SD	CV%	Min	Median	Max	Range
SBP	QD	1000	116	6.81	5.89	96	115	141	44
SBP	QOD	1000	111	6.81	6.16	91	110	136	44
SBP	Q2D	1000	113	7.78	6.92	90	112	141	51
SBP	Q7D	1000	114	5.83	5.14	97	114	135	38
SBP	Q10D	1000	111	7.78	7.04	88	110	139	51

Discussion

This case study suggests that intermittent dosing of amlodipine has limited impact on BP control. Due to its long half-life and sustained receptor binding, the drug maintains antihypertensive effects even with missed or delayed doses. These findings align with pharmacokinetic expectations and highlight the drug's forgiving profile compared to shorter-acting agents.

Importantly, results support flexibility in dosing schedules, which may improve adherence for patients who struggle with strict daily regimens. While this study is limited by its single-patient design, reliance on home monitoring, and simulation-based extrapolation, it provides preliminary evidence that alternative schedules may maintain efficacy.

Future studies with larger cohorts and prospective clinical trials are warranted to validate these findings and explore personalized dosing strategies.

Conclusion

Intermittent dosing of amlodipine, including schedules as infrequent as once weekly, did not significantly compromise blood pressure control in this case study. Monte Carlo simulations further support the robustness of antihypertensive effects across regimens. Personalized dosing approaches may enhance adherence and treatment outcomes compared to rigid once-daily prescribing.

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OPTIMIZING ATHLETIC PERFORMANCE THROUGH EVIDENCE-BASED NUTRITIONAL SUPPLEMENTATION: UPDATED EVIDENCE AND PRACTICAL APPLICATIONS

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Abstract

Optimizing athletic performance and post-exercise recovery necessitates a comprehensive approach that integrates dietary strategies with training demands and physiological responses. Athletes commonly use dietary supplements, although their usefulness varies depending on the supplement type, sport features, and individual reactivity. This narrative review critically assesses evidence from randomized controlled trials, systematic reviews, and meta-analyses published between 2015 and 2024, with a focus on supplements commonly used in individual sports. The findings show that creatine monohydrate consistently improves high-intensity power output and neuromuscular adaptation, whereas protein and essential amino acids help with muscle remodeling and recuperation.

Caffeine and β-alanine enhance cognitive focus, absorption capacity, and prolonged high-intensity performance. The importance of dietary nitrates and omega-3 fatty acids in lowering inflammation, accelerating healing, and improving cardiovascular function is further supported by new research. Notwithstanding these benefits, problems with optimal dosage, scheduling strategies, inter-individual variability, supplement quality, and regulatory compliance still exist. This study emphasizes the need for individualized, evidence-based supplementation plans that consider training phase, safety requirements, and sport specificity.

Keywords: *ergogenic nutrition, dietary supplements, sport performance, recovery strategies, creatine, amino acids, caffeine, omega-3 fatty acids, nitrates, individualized nutrition*

Introduction

Optimal physiological adaptation and competitive performance are becoming increasingly vital in modern sports, where modest gains can determine success. As training demands rise across all athletic disciplines,

nutritional supplementation has emerged as an important strategy for increasing performance and recovery. Supplement use among athletes has skyrocketed over the last two decades, owing mostly to emerging scientific data confirming the efficacy of certain compounds *(Maughan et al., 2018, Peeling et al., 2018)*. This increase reflects the rising recognition that nutrition is critical for exercise adaptation, metabolic efficiency, and post-exercise recovery *(Beck, 2015)*. However, despite widespread adoption, translating research into practice remains inconsistent, which is compounded by differences in study designs, demographic variables, and sport-specific demands on athletes *(Amawi, 2024)*.

The evidence for certain ergogenic compounds has been strengthened by recent systematic reviews, study designs, and systematic meta-analyses. Across a variety of demographics, it has been demonstrated that creatine, whey protein, essential amino acids, β-alanine, caffeine, and dietary nitrates enhance athletic performance or recovery *(Fernández Lázaro, 2024; Scapec, 2024; Morton, 2018; Saunders, 2016)*. One of the most researched supplements, creatine monohydrate, has been shown time and time again to enhance resistance training adaptations and high-intensity exercise performance *(Kreider, 2017; Wax, 2021)*. It has also been demonstrated that protein and essential amino acid supplements enhance muscle hypertrophy, strength, and recuperation *(Morton, 2018)*.

Caffeine *(Grgic, 2019; Pickering & Grgic, 2019; Scapec, 2024)* and β-alanine *(Saunders, 2016; Suszter, 2020)* are two supplements with evidence-based ergogenic potential. Caffeine improves strength, muscular endurance, and repeated-sprint ability, while β-alanine improves high-intensity performance through increased muscle carnosine availability. Omega-3 fatty acids, branched-chain amino acids (BCAAs), leucine, and various antioxidants have also received attention for their potential roles in reducing inflammation, oxidative stress, and muscle damage, thereby aiding recovery *(Clemente Suárez, 2023; Fernández Lázaro, 2024; Fouré & Bendahan, 2017; Martinho, 2022; Plotkin, 2021; Thielecke & Blannin, 2020)*. However, the evidence for these recovery-oriented supplements is more diverse and frequently constrained by methodological discrepancies or small study numbers.

Important uncertainties still exist despite advancements in the scientific literature. These include long-term safety concerns (*Garthe & Ramsbottom, 2020*), timing in relation to training, interindividual responsiveness (*Pickering & Grgic, 2019*), and optimal dosing protocols *(Ribeiro, 2021)*. Athletes must conform to international anti-doping regulations, therefore regulatory issues continue to be crucial to applied practice *(World Anti-Doping Agency, WADA, 2024*). These difficulties highlight the necessity of thorough, current, and sport-specific evidence syntheses.

Therefore, **the goal of this review** is to gather and analyze high-quality research that has been published between 2015 and 2024, with a focus on controlled trials, systematic reviews, and meta-analyses that look into nutritional supplements for athletic performance and recuperation. Dose-response correlations, sport-specific applications, interindividual variation, molecular pathways, and regulatory compliance are the main topics of discussion. In order to help practitioners, coaches, and athletes take nutritional supplements safely and effectively in sports, the review attempts to offer a thorough, evidence-based framework.

Research Methodology

This study was conducted as a narrative review using systematic search procedures to collect high-quality data on dietary supplements and athletic performance. The PubMed/MEDLINE, Scopus, Web of Science, and SportDiscus databases were searched extensively for publications published between January 2015 and December 2024.

Only systematic reviews, meta-analyses, and randomized controlled trials with competitive, well-trained, or healthy athletes were included. Eligible studies had to demonstrate objective performance or recovery outcomes, as well as well-specified supplementation protocols. Studies that used observational methodologies, clinical populations, multi-ingredient supplements without distinguishing individual effects, or had no performance-related outcomes were ex-

cluded. To locate more relevant articles, reference lists for relevant reviews and position statements were manually reviewed.

Supplement-Specific Evidence

Creatine monohydrate continues to be the most common ergogenic aid. Numerous meta-analyses and research studies reveal significant improvements in maximal strength, peak power, repeated sprint ability, and lean mass gains when combined with resistance training. *(Kreider et al., 2017; Mielgo-Ayuso et al., 2019; Wax et al., 2021)*. Lower dose regimens may have longer-term benefits, although effective protocols typically include a loading phase (≈20 g/day for 5–7 days) followed by maintenance (3–5 g/day) *(Ribeiro et al., 2021)*. According to position statements *(Kreider et al., 2017),* no consistent adverse effects have been detected at recommended doses, indicating long-term safety in healthy populations. Supplementing with protein, particularly whey or premium complete proteins, promotes muscle protein synthesis, recuperation, and adaptability in strength. *(Jäger et al., 2017; Beck et al., 2015)*.

Consuming 20–40 g of protein right after exercise improves the anabolic response. Protein supplementation is especially helpful during energy shortage or high-volume training stages. According to *Plotkin et, al* (2021), total daily protein consumption continues to be the dominant determinant for maximal hypertrophy or strength improvements, but isolated BCAA supplementation gives a slight benefit. Supplementing with beta alanine boosts intramuscular carnosine, improving buffering capacity and postponing tiredness during one to four minutes of high-intensity exercise *(Saunders et al., 2016; Suszter et al., 2020)*. Usually, protocols give 4–6 g daily for 4–8 weeks. Anaerobic and repeated sprint workouts yield the greatest advantages, whereas endurance activities yield mixed results. The most frequently reported side effect is mild paresthesia; in healthy people, there are no major adverse events.

Caffeine's ergogenic and neuromodulator characteristics have been extensively explored. Acute doses of 3–6 mg/kg administered 30–60 minutes before exercise consistently enhance anaerobic power, reaction time, perceived effort, and endurance performance *(Grgic et al., 2019)*. Recent RCTs *(Scapec et al., 2024)* suggest additional benefits for power output and muscle endurance. Variations in reaction between individuals may be influenced by genetic variants (such as CYP1A2), habitual intake, and stimulant sensitivity *(Pickering & Grgic, 2019)*. Long-term omega-3 supplementation (1–2 g/day EPA + DHA) supports anti-inflammatory responses, improves joint health, reduces muscular soreness, and may improve recovery *(Fernández Lázaro et al., 2024; Thielecke & Blannin, 2020)*.

Similarly, exercise-induced oxidative stress may be reduced by antioxidants and polyphenols, but excessive consumption may impair adaptive signaling *(Clemente Suárez, et al., 2023)*. There is little proof that omega-3 directly improves performance, but it is consistent for long-term musculoskeletal health and recuperation.

Particularly in recreational or lightly trained athletes, recent research indicates modest gains in time-trial performance and fatigue resistance. Supplementing with nitrate may be particularly helpful during multi-day tournaments or high-volume endurance training.

Results and Discussion

This review clearly demonstrates that, despite the wide availability of nutritional supplements marketed to enhance athletic performance, only a limited number are supported by strong and consistent scientific evidence. The results of the literature analysis indicate that **creatine monohydrate, caffeine, protein/essential amino acids, and β-alanine** currently represent the supplements with the most robust ergogenic support, whereas other supplements show moderate or context-dependent effects. Creatine monohydrate emerges as the most extensively researched and reliable ergogenic aid in sports nutrition. Experimental studies and expert consensus statements consistently report significant improvements in maximal strength, power output, and repeated high-intensity exercise performance. These benefits are primarily attributed to increased intramuscular phosphocreatine stores, enhanced ATP resynthesis, and

improved training quality over time *(Kreider et al., 2017; Wax et al., 2021)*. Collectively, these findings support the use of creatine as a foundational supplement, particularly in strength- and power-based sports. Protein intake and essential amino acids play a central role in supporting exercise-induced muscle hypertrophy and post-exercise recovery. Evidence indicates that **total daily protein intake** is a more critical determinant of adaptation than precise timing or isolated amino acid supplementation. Meta-analytical findings confirm that protein supplementation, when combined with resistance training, significantly enhances muscle mass and strength gains, especially in physically active and trained individuals (*Morton et al., 2018; Jäger et al., 2017)*. Caffeine demonstrates consistent ergogenic effects across a wide range of performance outcomes, including endurance capacity, muscular strength, power output, and reductions in perceived exertion. These effects are largely mediated through central nervous system stimulation, increased motor unit recruitment, and altered pain perception. However, substantial inter-individual variability exists, influenced by genetic factors, habitual caffeine intake, and dosing strategies, underscoring the importance of individualized supplementation protocols *(Grgic et al., 2019; Pickering & Grgic, 2019)*. β-Alanine supplementation has been shown to improve performance in high-intensity efforts lasting approximately 1–10 minutes by increasing intramuscular carnosine concentrations and enhancing buffering capacity against exercise-induced acidosis. The magnitude of these benefits depends on supplementation duration, total dose, and baseline carnosine levels, indicating that structured loading protocols are essential to maximize its ergogenic potential *(Saunders et al., 2016)*. Dietary nitrates, commonly consumed as beetroot juice, demonstrate moderate improvements in exercise economy and endurance performance, particularly in recreational and sub-elite athletes. These effects are attributed to increased nitric oxide bioavailability and improved mitochondrial efficiency. However, evidence in elite populations remains inconsistent, likely due to ceiling effects associated with already optimized physiological systems *(Peeling et al., 2018)*. Omega-3 fatty acids and antioxidant supplements primarily influence recovery-related outcomes, including inflammation, muscle soreness, and cellular stress, rather than directly enhancing performance. While these supplements may be beneficial during periods of intensified training or rehabilitation, emerging evidence suggests that chronic high-dose antioxidant supplementation may blunt training-induced physiological adaptations by attenuating exercise-related oxidative signaling pathways *(Clemente Suárez et al., 2023)*. Branched-chain amino acids (BCAAs) and isolated leucine are frequently promoted for muscle hypertrophy and recovery; however, current evidence indicates that their effects are inferior to those of complete protein sources containing all essential amino acids. Whole-protein supplementation more effectively stimulates muscle protein synthesis and supports long-term hypertrophic adaptations, particularly in resistance-trained individuals *(Fouré & Bendahan, 2017; Plotkin et al., 2021)*. Overall, **the findings of this review** confirm that nutritional supplementation can meaningfully enhance athletic performance only when grounded in strong scientific evidence, appropriate dosing, and sport-specific application. A major challenge remains the translation of laboratory-based findings into applied sport settings, where inter-individual variability, training status, and competitive demands substantially influence supplementation outcomes *(Amawi et al., 2024)*. Persistent misconceptions regarding supplement timing and synergistic combinations continue to exist, despite evidence suggesting that **total intake and chronic adaptation** are often more influential than acute timing strategies *(Ribeiro et al., 2021)*. Regulatory compliance also represents a critical consideration, as contamination risks and evolving anti-doping regulations pose ethical and career-threatening risks for athletes. Consequently, supplementation strategies should prioritize third-party tested products and evidence-based selection *(Maughan et al., 2018; WADA, 2024)*. **Although** this review synthesizes high-quality evidence, methodological heterogeneity across studies limits direct comparison and generalizability. Future research should place greater

emphasis on underrepresented populations, including female athletes, youth and master athletes, long-term safety outcomes, and precision nutrition approaches that account for individual genetic responsiveness.

Conclusions

This review confirms that only a limited number of nutritional supplements provide consistent and meaningful ergogenic benefits. **Creatine monohydrate, caffeine, protein/essential amino acids, and β-alanine** demonstrate the strongest evidence for enhancing strength, power, endurance, and training adaptations when appropriately dosed and applied. Other supplements show moderate or context-dependent effects, with limited direct influence on performance, and chronic high-dose antioxidant use may impair long-term adaptations. Overall, supplementation should support – not replace – sound nutrition and training practices and must be individualized according to sport demands and athlete characteristics. Given the potential risks related to contamination and anti-doping regulations, evidence-based selection and third-party testing remain essential for safe and effective supplement use.

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Section 3. Life Sciences

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MAKEUP FEATURES FOR DIFFERENT SKIN TYPES AND AGE GROUPS

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Abstract

The article is devoted to the subtleties of creating makeup that will match the characteristics of different skin types and ages. This is necessary to achieve an aesthetically harmonious and safe result. The article discusses the characteristics of dry, oily, combination, and sensitive skin and their impact on the choice of cosmetics, application techniques, and preparation of the skin for makeup. Special attention is paid to age-related changes, such as loss of elasticity, the appearance of wrinkles, changes in pigmentation, and skin texture. Makeup must be adapted to visually rejuvenate and, at the same time, preserve its natural appearance. The work systematizes recommendations for the selection of foundation products, decorative cosmetics, and tools, depending on the individual characteristics of the skin. Typical errors that can lead to a deterioration in appearance are also considered. The importance of an integrated approach is emphasized, which includes skin care, competent color correction, and moderation in the use of decorative accents. The results obtained can be useful for both makeup professionals and anyone who is interested in current trends in appearance care.

Keywords: *makeup, skin types, age characteristics, dry skin, oily skin, combination skin, sensitive skin, anti-aging makeup, decorative cosmetics, skin care, application technique, color correction*

Relevance of the study. Modern trends in the field of beauty emphasize the growing interest in an individual approach to makeup. This is due to the variety of skin types and pronounced age-related changes. Incorrectly, selected cosmetics and application techniques can not only spoil the appearance but also harm the skin, causing dryness, inflammation, and premature aging.

With the advent of new types of decorative cosmetics and the improvement of skin care technologies, it becomes especially important to have knowledge about the specifics of makeup for different skin types and age groups. This will help both professionals and makeup enthusiasts to create harmonious images that will not only please the eye but also take care of skin health.

The purpose of the study. The aim of this study is to identify and describe the features of makeup, considering skin type and age-related characteristics, and to develop practical guidelines for the selection of cosmetics and application techniques. Specifically, we aim to investigate the influence of physiological skin traits on the longevity and appearance of makeup. We also aim to analyze age-related changes that affect the visual perception of facial features and establish the most suitable approaches for creating natural and correctional makeup for various user groups.

Materials and research methods. The research examined scientific and educational materials on cosmetology, dermatology, and makeup art, as well as recommendations from modern cosmetics manufacturers. The analysis was based on a comparative study of the characteristics of different skin types and age-related changes that affect the structure and appearance of the skin. In the course of the work, methods of theoretical analysis, generalization, and systematization of information were used, as well as a descriptive method to identify the practical features of makeup. In addition, empirical observations obtained from the professional practice of makeup artists were taken into account. This allowed us to form an integrated approach to the choice of makeup techniques and products that takes into account individual skin characteristics and age.

The results of the study. The history of makeup is inextricably linked with the development of ideas about beauty, medical knowledge about the skin and technological progress in the cosmetics industry. In ancient civilizations such as Egypt, Greece, and Rome, cosmetics were used primarily for decorative and ritual purposes. At the same time, the individual characteristics of the skin were not taken into account. The focus was on the symbolism of color and status, and cosmetics often contained aggressive ingredients that could damage the skin.

In the Middle Ages, the use of cosmetics in Europe was limited, but during the Renaissance, interest in appearance increased again. During this period, the first ideas about skin types began to form, although they were primitive. Women with dry skin tried to use oily, oil-based formulations, while powdered matting products were used for oily skin. However, there was no systematic approach to makeup selection yet.

In the period from the 19th to the 20th century, significant changes took place in the field of dermatology and chemistry. The first classifications of skin types were developed: dry, oily, normal, and combination. This allowed a more conscious approach to the choice of cosmetics. At the same time, cosmetics began to be divided into age categories. It has been found that with age, the skin loses elasticity, becomes drier and more sensitive, which requires a special approach to textures and makeup techniques. For example, lighter and more moisturizing products designed specifically for mature skin have replaced dense powders and matte products.

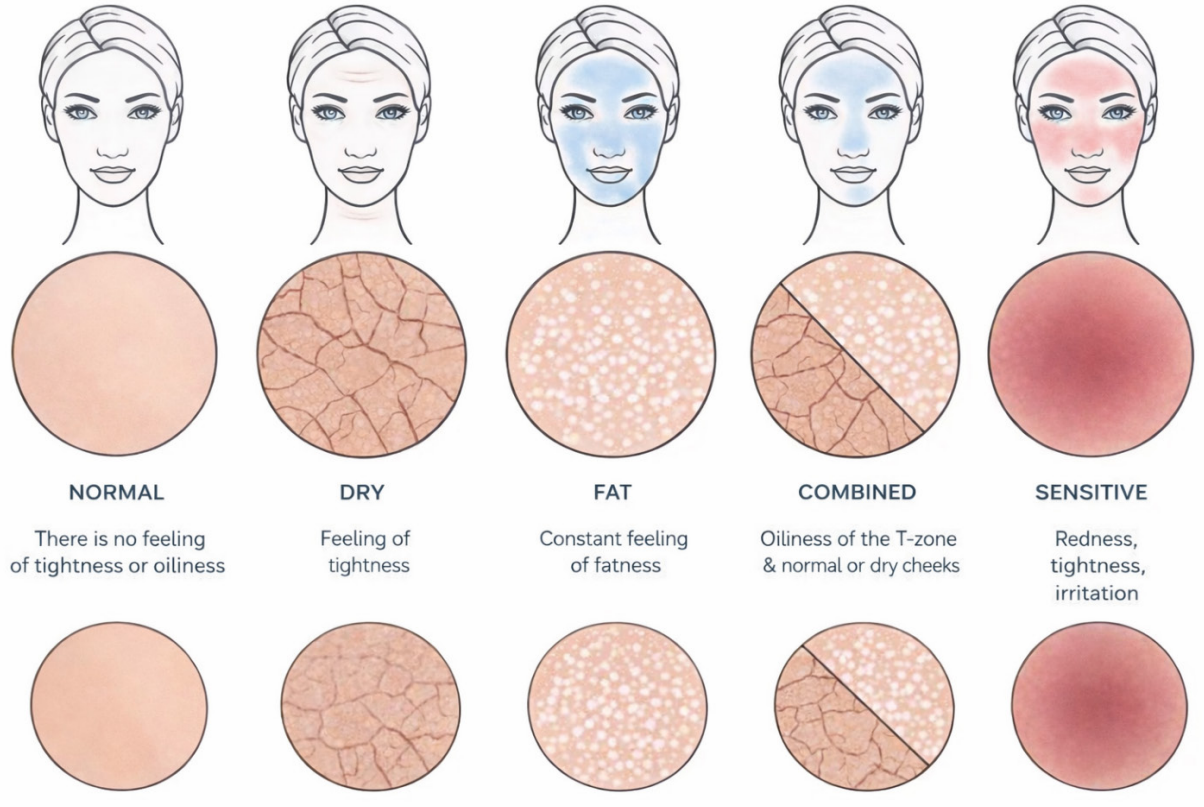
In the second half of the 20th century, the beauty industry experienced rapid growth. Professional makeup schools appeared where individual appearance characteristics were taken into account. Makeup became seen not only as a way to decorate but also as an effective tool for correcting age-related changes and skin imperfections. Special makeup techniques were developed, designed for both young skin, striving for naturalness, and mature skin, in order to visually rejuvenate it.

In the 21st century, the approach to makeup has become more individual. Now, not only the skin type and age are taken into account, but also its condition, sensitivity, presence of dermatological problems, as well as lifestyle. Modern products often combine decorative and care functions, including protection from ultraviolet rays (SPF), moisturizing, and anti-aging components.

Modern methods of studying makeup features for different skin types and age groups are based on advances in dermatology, cosmetology, and digital technologies.

Clinical studies of the skin play a key role, which include an analysis of the level of moisture, sebum production, elasticity, and sensitivity. With the help of dermatoscopy and computer diagnostics, specialists receive accurate data on the condition of the skin, which allows them to select makeup not only taking into account the basic skin type but also its current condition, for example, dehydration or a tendency to irritation (Fig. 1).

Figure 1. – *Characteristics of the main skin types*



One of the key methods is to test cosmetics both in the laboratory and in focus groups of different age categories. Manufacturers are studying how different textures and formulas affect the skin of teenagers, young adults and adults. For example, light gel and water bases are great for oily and young skin, providing its natural radiance (Kim B. et al., 2023). At the same time, creamy and richer textures are ideal for dry and age-related skin, providing additional nutrition and visually smoothing the tone (Table 1).

Table 1. – *Testing of cosmetics in laboratory conditions*

	Method	Characteristic
1	Microbiological testing	Analysis for bacteria and other pathogens to ensure product safety.
2	Clinical trials	Human testing conducted to evaluate the effectiveness and skin response to a product. As a rule, testing is carried out under the supervision of dermatologists.
3	Animal testing	Some companies resort to using animals to assess toxicity, but this method is becoming less popular due to ethical considerations.
4	Physico-chemical tests	Assessment of stability, pH, viscosity, flavor, and other characteristics.
5	Irritation tests	Assessment of the risk of allergic reactions and skin irritation.
6	Durability testing	Checking how the product performs over time under various storage conditions.

Digital technologies are also actively used in the field of makeup. Mobile applications and artificial intelligence systems analyze a photo of a face, determine skin type and age-related changes, and offer individual recommendations on product selection and application techniques. These systems take into account wrinkles, pigmentation, enlarged pores, and skin tone, which makes the selection of products more accurate.

In addition, augmented reality technologies are actively used. They allow you to "try on" makeup in real time without physically applying it. This simplifies the selection of shades and textures, reduces the risk of errors, and saves time. Combined with large databases and user reviews, such solutions form more objective and personalized recommendations, bringing the result closer to a professional level, even at home.

The creation of specialized cosmetics lines can be cited as practical examples. For instance, mattifying foundation products are being developed for oily skin that control sebum production and have a light texture so as not to clog pores (Dovzhanyn Y., 2024). Moisturizing bases with hyaluronic acid and oils have been created for dry skin, providing the necessary care. Age-related cosmetics use reflective particles and soft textures that do not accentuate wrinkles but create an effect of smoothness and radiance.

Furthermore, different makeup techniques have been developed for different age groups. Young girls are recommended to wear minimalistic makeup that adds naturalness. For mature skin, lifting techniques, corrective sculpting, and soft shading are suitable to avoid sharp lines.

Modern techniques combining scientific knowledge, technological achievements, and practical experience of makeup artists offer the most individual approach to makeup creation. They include the analysis of skin type, its condition, and even unique features, such as moisture levels or sensitivity, using digital diagnostic devices and applications. Special attention is paid to moisturizing the skin before applying makeup, as well-prepared skin looks smoother and more radiant. Foundation products are chosen with a light or medium coverage, often with caring components to provide the skin with additional hydration and protection.

Facial features are adjusted with delicate contouring and highlighting, which helps to restore volume and emphasize natural lines. As a result, age-related makeup does not hide, but harmoniously emphasizes natural beauty, creating a fresh and well-groomed image.

This allows you to select cosmetics and techniques more accurately. Not only are external features taken into account, but also the skin's reaction to various components. As a result, makeup not only looks aesthetically pleasing but also helps maintain skin health by adapting to its current needs and environmental conditions (Lee M., Han J., Kim E., 2019).

It is important to note that the difficulties in choosing makeup for different skin types and age groups are primarily due to a wide range of skin conditions and the frequent discrepancy between universal cosmetics and individual characteristics.

One of the main problems is the incorrect definition of skin type. For example, dehydrated skin is often mistaken for dry skin, although it requires special care and makeup. As a result, peeling or excessive shine may appear on it. For oily skin, the main problem is the durability of makeup. Excessive sebum production destroys the texture of foundation products, which leads to the effect of a "swollen" face. In addition, using dense products can lead to clogged pores and inflammation.

For people with combination skin, the main challenge is to balance the different areas of the face. Mattifying agents can overdry dry areas, while moisturizing agents can enhance the shine in the T-zone. If the skin is sensitive, this creates additional difficulties due to the high probability of irritation, allergic reactions, and redness. This limits the choice of remedies and requires the use of the most delicate formulas.

Age plays a significant role in the makeup selection process. In youth, the main difficulty lies in skin imperfections such as acne and post-acne. Dense coatings can exacerbate these problems. With age, the skin, on the contrary, loses elasticity, becomes thinner and drier, wrinkles and pigmentation appear. Many familiar products begin to emphasize the texture, clog into the folds, and visually

age the face. In addition, there is often a problem of choosing the wrong shades and textures. Too matte or dense products can make the face "flat" and heavy.

Difficulties also arise due to the lack of an individual approach in mass cosmetics and the lack of knowledge among users about application techniques. Improper product distribution, excess funds, or ignoring skin preparation lead to an unnatural result, regardless of the quality of cosmetics.

In our opinion, to successfully choose makeup for different skin types and age groups, a comprehensive and individual approach is needed. It includes a thorough diagnosis of the skin condition, proper care and adaptation of decorative products.

First, it is necessary to accurately determine not only the type of skin, but also its current condition. This applies to the level of moisture, sensitivity and the presence of inflammation. These factors directly affect the choice of textures and formulations of cosmetics.

Regular basic care is the foundation, as well-prepared skin allows makeup to lie flat and last longer. Therefore, the use of suitable cleansing, moisturizing and protective products should be a mandatory step in the care process.

It is important to keep in mind your skin type in order to choose the most suitable products. For oily skin, light mattifying textures are suitable to help regulate sebum production. Dry skin needs richer and more nutritious formulas. Sensitive skin requires hypoallergenic products with a minimum amount of aggressive ingredients. Combination skin needs balanced care that takes into account the characteristics of different areas of the face.

With age, the skin loses elasticity and moisture, which makes it especially important to use products with moisturizing and anti-aging components such as hyaluronic acid, antioxidants, and peptides. In makeup, this is reflected in the choice of lighter, radiant textures that do not focus on wrinkles and irregularities.

For oily skin, light, non-comedogenic formulas, mattifying primers, and tonal products with sebum control will be the ideal solution. However, it is important to avoid excessive drying so as not to provoke even more sebum production. With dry and dehydrated skin, the emphasis shifts to intensive hydration and the use of creamy textures that do not emphasize peeling and create a more natural coating. Combination skin requires a zonal approach, when different products are applied to different areas of the face, which allows you to create a balanced and harmonious image without overload.

For example, mattifying agents that control sebum production are suitable for the T-zone. But on dry areas, such as cheeks and temples, it is better to use moisturizing and nourishing formulas.

When applying makeup, it is also important to consider this feature: dense textures should be used with caution in areas prone to greasiness to avoid congestion. On dry areas, choose lighter and more radiant products that will not emphasize peeling. This differentiated approach will help achieve a more natural and lasting result, while maintaining a balance between matte and moisturized skin radiance. For sensitive skin, it is recommended to choose hypoallergenic cosmetics with a minimum amount of irritating components. Testing should be carried out before full use of the products.

In age-related makeup, heavy and excessively matte textures should be avoided. It is better to give preference to light, reflective products that visually smooth the skin and do not emphasize wrinkles. Additionally, it is important to adjust the makeup technique. Instead of a dense coating, thin layers should be used, and the products should be gently blended.

Furthermore, a significant improvement in the outcome is provided by training in basic makeup techniques and understanding the principles of product combinations. Even high-quality cosmetics can look unflattering if applied incorrectly, so it's important to learn how to use them properly. Personalization, attention to skin changes as we age, and regular evaluation of the products we use can help minimize common problems and achieve a natural, harmonious look.

Conclusions

The specifics of makeup for different skin types and age categories clearly demonstrate that there is no single universal solution. To

achieve an effective result, it is necessary to take into account individual skin characteristics and age-related changes.

Properly selected tools and techniques allow not only to favorably emphasize the advantages of appearance but also to hide flaws, creating a natural and aesthetic image. Skin care is the basis of high-quality makeup, as the condition of the skin directly affects the durability and result of decorative cosmetics. With age, makeup requirements change, which requires the use of textures that are more delicate, proper product distribution, and an emphasis on visual rejuvenation.

Thus, an individual approach, understanding of the specifics of the skin and mastery of modern makeup techniques become key factors in creating a harmonious and professional image.

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Section 4. Veterinary medicine and zoology

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CYNOLOGY AS A BASIS FOR THE PREVENTION AND BEHAVIORAL CORRECTION OF DISORDERS IN DOMESTIC DOGS

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Abstract

This article discusses cynology as the basis for the prevention and correction of behavioral problems in domestic dogs. It reveals the theoretical aspects of this science, which help to better understand the behavior of dogs. In particular, ethology, breed classification, breeding, features of early development and modern approaches to education are considered. The causes and most common groups of behavioral disorders in domestic dogs are also revealed. Special attention is paid to the preventive role of cynology. It consists in the early socialization of dogs, taking into account their individual and breed characteristics, proper organization of the environment, training of owners, and the use of humane methods of interaction with animals. The practical aspects of the application of cynological knowledge for the prevention and correction of problematic behavior are considered. In addition, current problems and prospects for the development of cynological prevention are discussed. As a result, it was found that cynology is an important scientific and practical basis for maintaining the well-being of dogs, preventing persistent behavioral disorders, and improving the quality of interaction between dogs and humans.

Keywords: *cynology, domestic dogs, dog behavior, behavioral disorders, prevention of behavioral disorders, behavioral correction, socialization of dogs, dog training, animal welfare, methods of behavior correction.*

Relevance of the study

The relevance of this study stems from the dog's important place in modern human life as a faithful friend and companion. Therefore, issues related to its maintenance, upbringing, and adaptation to family life are of great practical importance. The widespread use of domestic dog breeding makes the problems that arise in the formation of stable, socially acceptable, and safe behavior in animals especially important.

Particular attention to this topic is warranted because behavioral disorders in domestic dogs are a common problem that

affects not only the animals themselves but also their owners. Undesirable behavior complicates the maintenance of a dog at home, reduces the quality of interaction between humans and animals, and often causes the abandonment of a pet. Scientific literature notes that such violations are closely related to the welfare of animals, their level of socialization, conditions of detention, and the quality of educational work.

The relevance of this study is strengthened by the fact that a significant number of behavioral issues can be avoided with a well-informed and responsible approach to dog ownership. Early socialization, understanding of breed characteristics, appropriate training methods, and awareness of canine behavior all contribute to reducing the risk of behavioral disorders and ensuring a more harmonious relationship between dogs and humans. Recent research has also shown that gentle, positive reinforcement training methods are more effective and beneficial for a dog's well-being than harsher methods. In this context, cynology serves not only as an area of specialized knowledge about dogs but also as a crucial practical resource for preventing and addressing behavioral issues in domestic dogs.

The purpose of the study

The aim of this study is to examine cynology as a scientific and practical foundation for the prevention and correction of behavioral issues in domestic dogs. It also aims to identify the significance of cynological knowledge in avoiding problematic behaviors, selecting appropriate correction methods, and enhancing the well-being of these animals.

Materials and research methods

Our research is based on open scientific publications, professional recommendations from cynological and veterinary organizations, as well as data from modern research on the behavior of domestic dogs, the causes of behavioral problems and methods of their prevention and correction.

In the course of our work, we used various methods, including analyzing scientific literature, summarizing the experience of professionals, comparing approaches to the prevention and correction of behavioral disorders, as well as systematizing information about the causes, forms of manifestation, and ways to prevent behavioral problems in domestic dogs.

The results of the study

The theoretical foundations of cynology are fundamental to understanding dog behavior. A domestic dog's behavior depends on many factors: its origin, heredity, early development, living conditions, health status, and experience of interaction with humans. Modern scientific research considers the dog a social animal whose behavior was formed during domestication and subsequent breeding. Therefore, it is impossible to analyze a dog's behavior without regard to its biological and breed characteristics (Tancredi D., Cardinali I., 2023).

The main theoretical aspects of cynology include ethology, breed classification, fundamentals of breeding, anatomical and physiological features of dogs, and principles of learning. Ethology is a science that studies animal communication, behavioral signals, and mechanisms of adaptation and social interaction. Breed classification is important because breeds were formed according to their working functions, which affects not only their external characteristics but also their stable behavioral features. The official FCI classification groups breeds according to their origin and functional purpose. This allows us to better understand the typical patterns of activity, reaction, and interaction of dogs with their environment.

The most important theoretical aspects of cynology include ethology, breed classification, the basics of breeding, anatomical and physiological characteristics of dogs, and the principles of training. Ethology studies the forms of communication, behavioral signals, adaptation mechanisms, and social interaction of dogs. Breed classification plays an important role, as breeds were formed depending on their working purpose. This affects not only their external characteristics but also their stable behavioral patterns. The official classification developed by the FCI (International Cynological Federation) unites breeds into groups according to their origin and functional purpose. This allows us to better understand the typical patterns of activity,

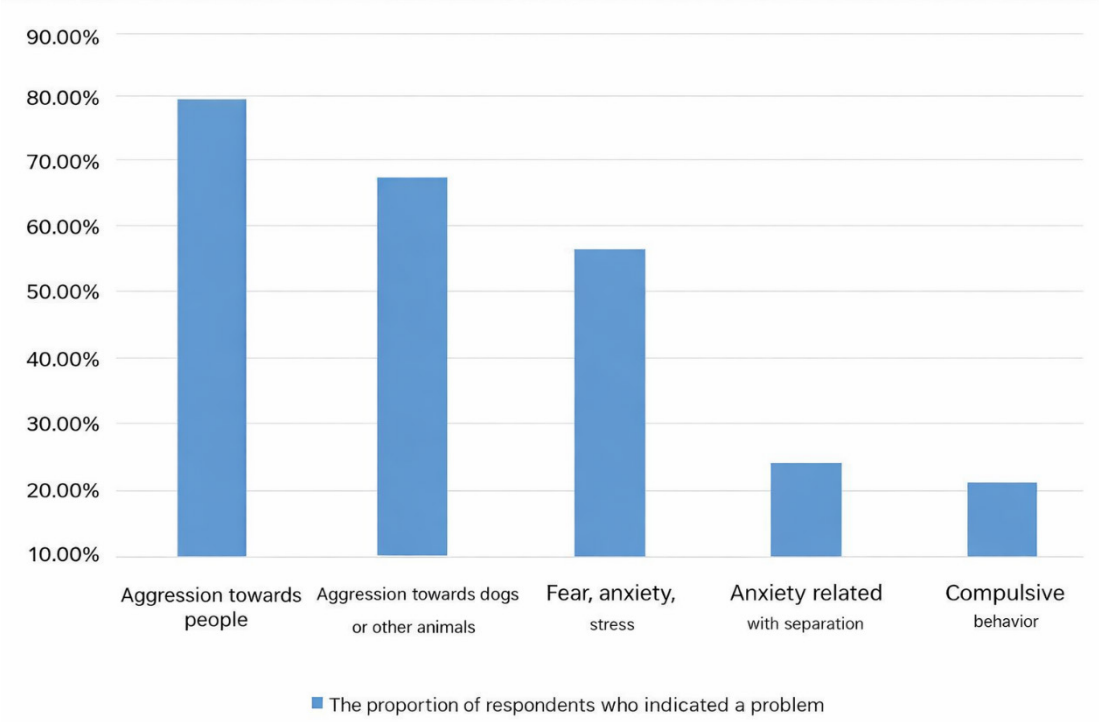
reaction, and interaction of dogs with their environment.

The breeding approach also plays an important role. If it is not right to choose a pair, especially if the producers have an unstable psyche, this can lead to the offspring developing undesirable behavioral qualities. That is why not every dog can be allowed to breed. The evaluation of producers should take into account not only the conformity of their appearance to the breed type, but also the peculiarities of behavior, as well as the stability of the psyche. Exhibitions and other zootechnical events where an expert comprehensively evaluates an animal, including its behavior, serve as an important basis for this.

In modern veterinary behavioral medicine, behavioral disorders in domestic dogs are defined as conditions in which an animal's behavior goes beyond the usual adaptive response, causing it discomfort, making it difficult to care for it, and posing a danger to others. It is important to distinguish normal but undesirable behavior from disorders. Normal but undesirable forms include, for example, digging, excessive chewing of objects, tagging, playful biting, or stalking. These actions are part of the dog's natural behavior, but they can become a problem in everyday life. Pathological or clinically significant disorders include reactions based on fear, anxiety, overexcitation, and loss of self-control (Borns-Weil S., 2025).

The classification of behavioral disorders usually includes several main groups (Figure 1).

Figure 1. *The main groups of behavioral disorders in domestic dogs*



A source: (Miranda Hitchcock et al., 2024)., a study of factors related to behavioral euthanasia of domestic dogs, n = 690.

To understand how disorders are formed, it is necessary to take into account another important point: not every undesirable action of a dog is a manifestation of a separate behavioral disorder. In some cases, the problem arises due to the discrepancy between the natural activity of the animal and the conditions of its maintenance. Therefore, when assessing the situation, it is always necessary to take into account the history of the dog's development, the context of the symptoms, its state of health, and the nature of interaction with the owner. This comprehensive approach makes it possible to distinguish a behavioral disorder from errors in content or learning (Table 1).

Table 1. *The main causes and clinical significance of behavioral disorders in dogs*

The causal factor	What open sources indicate
Hereditary predisposition	It may increase the risk of fear, anxiety, aggression, and violations of self-control.
Insufficient early socialization	It promotes worse adaptation to people, animals and new conditions.
Medical reasons	Pain, illness, and neurological disorders can change behavior.
Traumatic events and stress	It leads to the formation of stable reactions of avoidance, anxiety and aggression.
Unintended reinforcement	It can reinforce undesirable reactions such as barking, begging, stealing items, and others.

A source: author's development

Cynology is seen as the foundation for preventing behavioral issues in domestic dogs, as the prevention of problematic behaviors does not start when severe symptoms occur, but rather at earlier stages of dog care. Professional guidelines suggest that prevention should take into account the age, size, lifestyle, and breed characteristics of the dog as well as their life stage. This approach allows for the selection of a suitable regimen, level of stress, training method, and ways to interact with the animal in advance (Creevy K. E., at al., 2019).

From a practical perspective, the preventive value of dog training is primarily related to the proper organization of the environment and the controlled development of skills. The American Veterinary Society of Animal Behavior (AVSAB) emphasizes that early and adequate socialization, as well as positive training programs, can significantly reduce the risk of behavioral issues and improve the bond between dogs and humans. These same recommendations highlight the importance of safely conditioning dogs to restrictions and providing a place to rest: using pens, crates, or other quiet containment methods is seen as a way to reduce stress during both domestic and veterinary visits (AVSAB, 2019).

The preventive role of canine training is also evident in the fact that a dog's behavior is not seen in isolation, but rather as a product of the combined efforts of the breeder, owner, and professional. It is emphasized that socialization must begin early and continue throughout the dog's daily life, with both the breeder and owner sharing responsibility for this. Importance is placed on educating owners during initial preventive visits with a veterinarian, where principles of care, familiarization with new surroundings, and avoidance of fear can be discussed in a timely manner.

Another preventive measure is the training of the owner. Participation in puppy training classes is linked to a more positive development of manageability and human-dog relationships. Factors that increase the likelihood of attending these classes include the owner's previous intention to receive training, their first experience owning a dog, and receiving information when purchasing a puppy. This demonstrates that prevention depends not only on the dog, but also on the owner's preparedness.

For practice, it is important to focus on prevention for those problems that dog owners actually encounter most frequently. According to a study published in Scientific Reports, the most common behavioral and management difficulties include jumping on people, chasing animals, territoriality, excessive arousal, socialization difficulties, and a lack of time for owners. These findings confirm that canine prevention should involve not only training in basic commands but also the development of self-control, calm behaviors, safe interactions with people, and adaptation to urban and domestic environments (Gillet L., Simon B., Kubinyi E., 2024).

Cynological methods for behavioral correction of disorders in domestic dogs involve a set of techniques designed to change undesirable behaviors, develop stable and useful skills, and reduce emotional stress for the animal. These techniques are based on modern methods that encourage desirable behavior, gradually teach new skills, manage the environment, and take into account the individual characteristics of each dog (Table 2).

Table 2. *The main cynological methods of behavioral correction of disorders in domestic dogs*

Correction method	The essence of the method	What violations are used for
Positive reinforcement	Encouraging desirable behavior	Anxiety, fear, agitation, uncontrollability
Desensitization	Gradual decrease in sensitivity to an irritant	Fears, phobias, and anxiety reactions
Control conditioning	Forming a positive reaction to a previously unpleasant stimulus	Fear, anxiety, negative reaction to people, animals, situations
Environment management	Elimination of provoking factors	Destructive behavior, agitation, conflicts
Redirecting behavior	Replacing an undesirable action with an acceptable one	Chewing objects, excessive activity, grabbing
Self-control training	Formation of calm and controlled behavior	Impulsivity, jumping, jerking, overexcitation
Correction of the activity mode	Selection of sufficient physical and mental activity	Hyperactivity, anxiety, destructive behavior
Exclusion of medical reasons	Consideration of health status when assessing behavior	Aggression, anxiety, sudden changes in behavior

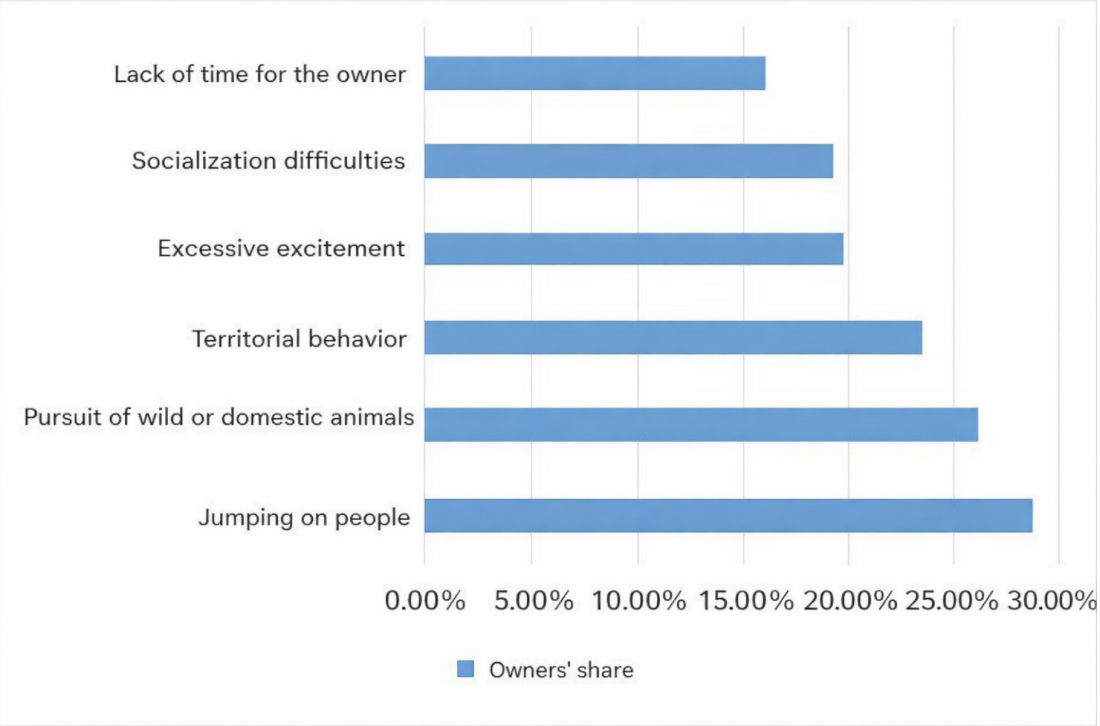
A source: author's development

The practical application of canine knowledge involves working not only with a specific symptom but also with the overall organization of a dog's daily life. This includes establishing a walking routine, managing stimuli, teaching essential skills, helping the dog develop the ability to calmly handle everyday situations and social interactions, and regularly assessing the impact of the owner's actions on problematic behavior. Research indicates that many common difficulties experienced by owners are related not to rare medical conditions but rather to common behavioral challenges.

In a survey of dog owners, the most common challenges included jumping on people, chasing other animals, territorial behavior, excessive excitement, difficulty socializing, and a lack of time for their owners (Figure 2). This data is important for practitioners, as it shows the areas that preventive and corrective programs should focus on: developing self-control, creating calm interactions with humans, guiding walking behavior, and helping dogs adapt to their daily environment.

Information about the prevalence of problematic behavior in domestic dogs is also important. In one survey, owners most often mentioned problems such as excessive activity, fearfulness, destructive behavior, aggression towards strangers, and a tendency to leave or wander. These data confirm that dog training should include both correction of emotional disorders and training in behavior control in everyday life.

Figure 2. *The most common practical problems of dog behavior and management according to the survey of owners*



A source: (Gillet L., Simon B., Kubinyi E., 2024)

However, the main problem in the development of canine prevention remains the discrepancy between scientific methods and the practice of daily dog handling. Although professional organizations recommend the use of incentive methods, the literature notes that owners still often resort to aversive methods of influence. This may be due to a lack of knowledge, well-established everyday beliefs about training, and difficulties in finding qualified help.

Another problem is that many behavioral difficulties in dogs are discovered after they become part of the animal's daily life. Behavioral management guidelines emphasize the importance of early identification of risk factors, discussion of behavior at preventive checkups, and inclusion of behavior assessment in the regular dog care process. One of the promising areas is closer cooperation between dog handlers, veterinary specialists, and owners. In addition, it is necessary to expand access to early counseling and training programs for owners so that they can receive timely help and support in solving behavioral problems.

The prospects for the development of canine prevention are to continue to apply humane training methods, conduct early behavioral counseling, implement socialization programs, and provide individual support for dogs at all stages of their lives. Modern experts believe that training should be aimed not only at obedience but also at maintaining the well-being of the dog, the stability of its behavior, and the quality of the relationship between animal and human. This approach seems to be the most reasonable for the further development of prevention and correction of behavioral disorders in domestic dogs.

Conclusions

Cynology is an important field of science and practice devoted to the prevention and correction of behavioral problems in domestic dogs. A dog's behavior is determined by a variety of factors, including heredity, physiology, housing conditions, and social environment, so its assessment and adjustment require a comprehensive approach. Research shows that many behavioral disorders are associated with insufficient socialization, maintenance errors, lack of systematic training,

failure to take into account the individual characteristics of the dog, and the untimely identification of risk factors. In this regard, preventive work is of particular importance, including early socialization, proper environmental management, owner training, and the use of methods based on encouragement and stress reduction. The practical application of knowledge gained in cynology allows not only to correct already formed disorders but also to prevent their development at an early stage.

The prospects for further development of canine prevention are related to the introduction of humane training methods, increasing the availability of early counseling, and strengthening cooperation between dog owners, dog handlers, and veterinarians.

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Contents

Section 1. Preventive medicine

Rory Hu

DISCOVERY OF SMALL MOLECULE INHIBITORS OF MAO-B FOR ALZHEIMER'S DISEASE USING PHARMACOPHORE-BASED VIRTUAL SCREENING 3

Matthew Shang

STATISTICAL MODELING OF INTERMITTENT AMLODIPINE DOSING USING MONTE CARLO SIMULATION AND REAL-WORLD BLOOD PRESSURE DATA 19

Section 2. Physiology

Msc. Narvina Sinani, Prof.Asc.Dr.Najada Quka, Prof Asc Dr. Rigerta Selenica

OPTIMIZING ATHLETIC PERFORMANCE THROUGH EVIDENCE-BASED NUTRITIONAL SUPPLEMENTATION: UPDATED EVIDENCE AND PRACTICAL APPLICATIONS. 23

Section 3. Life Sciences

Korchynska Alina

MAKEUP FEATURES FOR DIFFERENT SKIN TYPES AND AGE GROUPS 29

Section 4. Veterinary medicine and zoology

Nesterenko Viktoriia

CYNOLOGY AS A BASIS FOR THE PREVENTION AND BEHAVIORAL CORRECTION OF DISORDERS IN DOMESTIC DOGS. 35