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ORIGINAL RESEARCH

ADME properties, bioactivity and molecular docking studies of 4-amino-chalcone derivatives: new analogues for the treatment of Alzheimer, glaucoma and epileptic diseases

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Abstract

In this study, in vitro inhibition effects of (E)-1-(4-aminophenyl)-3-(aryl) prop-2-en-1-one (4-amino-chalcones) derivatives (3a–o) on acetylcholinesterase (AChE) enzyme and human erythrocyte carbonic anhydrase I and II isoenzymes (hCA I- II) were investigated. And also, the biological activities of 4-amino-chalcone derivatives against enzymes which names are acetylcholinesterase (PDB ID: 1OCE), human Carbonic Anhydrase I (PDB ID: 2CAB), human carbonic anhydrase II (PDB ID: 3DC3), were compared. After the results obtained, ADME/T analysis was performed in order to use 4-amino-chalcone derivatives as a drug in the future. Effective inhibitors of carbonic anhydrase I and II isozymes (hCAI and II) and acetylcholinesterase (AChE) enzymes with Ki values in the range of 2.55 ± 0.35–11.75 ± 3.57 nM for hCA I, 4.31 ± 0.78–17.55 ± 5.86 nM for hCA II and 96.01 ± 25.34–1411.41 ± 32.88 nM for AChE, respectively, were the 4-amino-chalcone derivatives (3a–o) molecules.

Keywords 4-Amino-chalcones · Carbonic anhydrase · Acetylcholinesterase · Molecular docking

Introduction

Acetylcholine is a neurotransmitter substance secreted from the synapses of autonomic ganglia and the ends of nerve strands laying the skeletal muscle. Acetylcholinesterase (AChE; EC 3.1.1.7) is a nonspecific enzyme that hydrolyzes lipotropic acetylcholine in the tissues, free or combined with phospholipids.In other words, acetylcholinesterase functions around by removing the chemicals that accumulate in front of the nerve end and removing them from there. Thus, a possible malfunction in nerve conduction does not occur (Göcer et al. 2017; Ökten et al. 2020; Çakmak et al. 2020).

One of the most important causes of Alzheimer's disease is the decrease in the amount of acetylcholine in the brain (Göcer et al. 2017).

AChE inhibitors (Donepezil, Rivastigmin) are widely used for Alzheimer's patients to live as high quality (Göcer et al. 2013, 2015). However, such drugs with inhibitory effects cause side effects such as gastrointestinal disorders and hepatotoxicity. For this reason, AChE inhibitors, which are both effective and safe, as well as especially natural, have become more and more important in recent times (Gülçin et al. 2020; Timur et al. 2019).

Carbonic anhydrase inhibitors are among the most potent drugs that reduce the intraocular pressure used in the treatment of eye diseases. These have been recently used for reducing intraocular pressure, topical and is used systemically. Acetazolamide, a systemic inhibitor of carbonic anhydrase, was first used in 1954 by Becker, Grant, Trotter, Breinin and Gürtz to reduce intraocular pressure in glucose disorder (Becker 2020; Kim et al. 2019; Supuran 2019). In addition, acetazolamide is the most used inhibitor of the carbonic anhydrase enzyme. Recently, there has

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been a search for inhibitors for hCA isoenzymes in structures other than sulfonamides. Inhibitor development and synthesis studies have been increased, especially for use in drug design development.

Recently, in many studies, the importance and place of theoretical studies has increased. Experimental studies conducted in these studies are guiding (Tüzün et al. 2018, 2020; Bilgiçli et al. 2020a, b; Douche et al. 2020). Theoretical studies are preferred because they are very fast, and their cost is cheap. Among the theoretical methods, the most common and fastest molecular docking method was used to compare the biological activities of 4-amino-chalcone derivatives (**3a–o**) against enzymes (Taslimi et al. 2020). These enzymes are acetylcholinesterase (AChE) (PDB ID: 1OCE) (Cheung et al. 2013), human Carbonic Anhydrase I (hCA I) (PDB ID: 2CAB) (Alterio et al. 2010), human carbonic anhydrase II (hCA II) (PDB ID: 3DC3) (Ivanova et al. 2015). ADME/T (Absorption, distribution, metabolism, excretion, and toxicity) analysis was then performed to investigate the drug availability of 4-amino-chalcone derivatives (**3a–o**). The parameters obtained as a result of this ADME/T analysis theoretically examined the biological effects and reactions of this molecule in human metabolism.

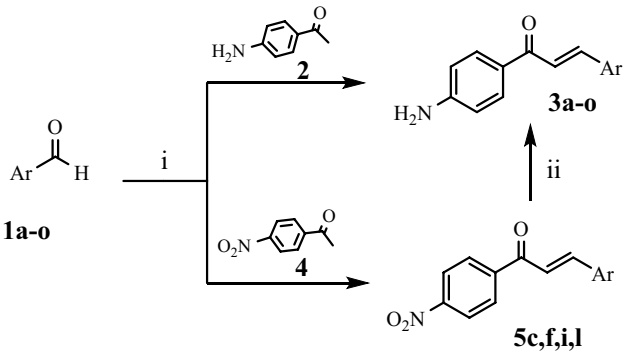
Whether hCA I and II isoenzymes and AChE, these three enzyme systems are of great importance for human health. Changes in the level of hCA in human erythrocytes are associated with many metabolic disorders such as diabetes, edema and hypertension (Bayindir et al. 2019). AChE enzyme, on the other hand, they are the enzymes responsible for the emergence of many neurological diseases, including Alzheimer's (Güzel et al. 2019).

In the scope of our study, the inhibition properties of 4-amino-chalcone derivatives (**3a–o**) were investigated by using them as inhibitors. Depending on the results obtained, these molecules or their derivatives are used in drug designs in terms of usability in the treatment of many diseases. We anticipate that it will shed light and make significant contributions in the field of pharmacology.

Results and discussion

Chemistry

4-Amino-chalcone derivatives (**3a–o**) were resynthesized from the Claisen-Schmidtcondensation of the benzaldehyde derivatives (**1a–o**) with 4-aminoacetophenone (**2**) according to the published procedure (Koçyiğit et al. 2018; Gürdere et al. 2020). (Scheme 1, Table 1). All spectroscopic data are in good agreement with the published data.



Scheme 1 Reagents and conditions: (i) NaOH, C_2H_5OH, 0 °C, 3 h, (ii) $SnCl_2{\cdot}2H_2O$, C_2H_5OH, reflux, 2 h

Biochemical studies

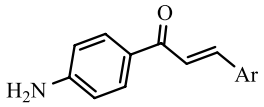
Inhibition of metabolic enzymes was investigated, and their results were reported as follows.

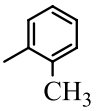
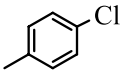
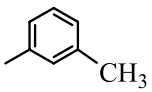
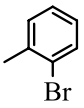
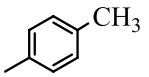
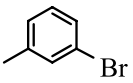
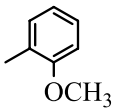
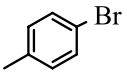
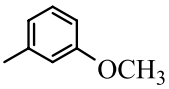
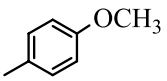
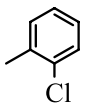
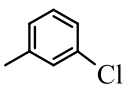
In this study, the compounds **3a–o** were screened against the AChE enzyme due to significant reports on AD of phenolic natural or synthetic compounds. IC_{50} and K_i values of the reference drug Tacrin were 1143.31 nM (IC_{50}) and 858.85 ± 12.11 nM (Ki) towards AChE, as shown in Table 2. The compounds inhibited the AChE enzyme in nanomolar concentration in the range of K_i values of 96.01 ± 25.34–1411.41 ± 302.88 nM and with IC_{50} values of 179.71—1048.41 nM. The compounds **3a** and **3d** were found potent AChE inhibitors with the Ki values of 96.01 ± 25.34 nM and 156.45 ± 66.48 nM, respectively, while the compound was the least inhibiting compound with the highest K_i value of 1411.41 ± 302.88 nM. On the other hand, the compound **3e** was also considered as one of the potent inhibitors with the lowest IC_{50} value of 179.71 nM against AChE (Figs. 1, 2). The Table 2 showed that the K_i values of reference drug AZA were 83.90 ± 19.71 nM and 104.60 ± 27.60 nM, whereas the IC_{50} values of AZA were 97.30 nM and 115.50 nM towards hCA I and II, respectively. Ki values of **3a–o** were calculated as 2.55 ± 0.35–11.75 ± 3.57 nM for hCA I, 4.31 ± 0.78–17.55 ± 5.86 nM for hCA II.

Glaucoma with high intraocular pressure is one of the most important eye diseases. It causes blindness with a rate of 15–20%. hCA II in the eye retina is the primary cause of intraocular pressure formation. The most important method to eliminate this disease is to inhibit hCA II activity. For this purpose, acetazolamide and heteroaromatic sulfonamides have been used as inhibitors for many years (Ellman et al. 1961; Lineweaver and Burk 1934; Verpoorte et al. 1967).

Acetyl CoA is a product formed as a metabolic product of pyruvate occurring in glycolysis. Alzheimer's disease occurs as a result of decreased neurotransmitters in the brain. The most decreasing neurotransmitter in this disease

Table 1 Chemical structures of compounds



Compound	Ar	Compound	Ar
3a		**3i**	
3b		**3j**	
3c		**3k**	
3d		**3l**	
3e		**3m**	
3f		**3n**	
3g		**3o**	
3h			

is widespread dementia and neurodegenerative disease. Alzheimer's disease function of memory.

It was found as disorder. The decrease in the level of acetylcholine in the brain is the biggest biochemical factor of this disease. There is no cure for this disease. The treatments applied today are aimed at eliminating the symptoms of this disease. There is no treatment method that eliminates it. AChE inhibitors such as Rivastigmine and Donepezil are generally used for this purpose (Kocyigit et al. 2017; Güzel et al. 2019; Ökten et al. 2019).

The presence of some unwanted negative physiological effects of these drugs in patients has made the discovery of new inhibitors important.

Molecular docking results

Molecular docking calculations were made to compare the biological activities of 4-amino-chalcone derivatives enzymes against proteins. Molecular docking calculation results of 4-amino-chalcone derivatives appear to be in great agreement with the experimental results (Aktas et al. 2020a, b; Gedikli et al. 2021). In the docking calculations of 4-amino-chalcone derivatives, numerical values of calculated many parameters as a result of docking calculations of molecules and enzymes support this situation. The most important factor affecting the numerical values of the parameters calculated from the interaction of amino-chalcone derivatives with enzymes is the interaction (Tüzün et al. 2021). Many chemical interactions occur between amino-chalcone derivatives with enzymes. As these chemical interactions increase, the biological activities of 4-amino-chalcone derivatives appear to increase. These interactions have many interactions such as hydrogen bonds, polar and hydrophobic interactions, π-π and halogen bonds (Sayin and Karakas 2017, 2018a; b; Sayin and Üngördü 2018, 2019; Üngördü and Sayin 2019; Jayarajan et al. 2020). As a result of calculations, the interactions of molecules with enzymes are given in Figs. 3, 4,

Table 2 Inhibition results of novel 4-Amino-chalcone derivatives (**3a-o**) on carbonic anhydrase and acetylcholinesterase

Compounds	IC_{50} (nM)						K_i (nM)		
	hCA I	r^2	hCA II	r^2	AChE	r^2	hCA I	hCA II	AChE
3a	8.35	0.9717	9.11	0.9810	261.91	0.9639	5.46 ± 1.32	9.68 ± 2.51	156.45 ± 66.48
3b	8.15	0.9658	9.01	0.9569	408.61	0.9817	11.75 ± 3.57	17.55 ± 5.86	259.33 ± 35.95
3c	5.87	0.9580	6.86	0.9973	700.01	0.9872	4.26 ± 0.85	5.76 ± 0.91	514.47 ± 95.66
3d	7.01	0.9960	9.36	0.9724	222.47	0.9848	6.94 ± 1.83	13.21 ± 4.07	96.01 ± 25.34
3e	4.35	0.9575	5.02	0.9953	382.45	0.9811	4.62 ± 0.82	5.38 ± 1.23	474.15 ± 70.66
3f	3.82	0.9797	4.84	0.9784	179.71	0.9668	2.81 ± 0.18	4.31 ± 0.78	159.62 ± 68.17
3g	8.25	0.9639	10.51	0.9528	1048.41	0.9689	10.26 ± 1.47	11.80 ± 3.95	456.80 ± 114.41
3h	7.37	0.9917	8.55	0.9768	548.26	0.9905	7.31 ± 2.98	7.22 ± 2.26	218.63 ± 59.47
3i	5.37	0.9991	6.66	0.9896	758.21	0.9490	6.14 ± 1.42	6.04 ± 1.52	1411.41 ± 302.88
3j	6.35	0.9839	6.93	0.9683	898.83	0.9691	3.97 ± 0.91	9.93 ± 2.51	361.63 ± 73.80
3k	4.91	0.9965	7.29	0.9543	327.21	0.9753	4.87 ± 0.83	7.91 ± 1.88	299.77 ± 47.33
3l	6.61	0.9660	8.88	0.9703	564.33	0.9692	10.04 ± 1.80	6.23 ± 2.20	337.48 ± 99.43
3m	3.66	0.9722	5.82	0.9773	595.36	0.9908	2.55 ± 0.35	6.94 ± 1.55	495.94 ± 72.81
3n	5.54	0.9847	7.45	0.9832	756.55	0.9933	6.56 ± 1.96	5.91 ± 1.01	619.81 ± 85.46
3o	7.45	0.9865	8.46	0.9425	488.02	0.9518	5.04 ± 1.55	10.18 ± 0.85	285.20 ± 86.92
AZA	97.304	0.9889	115.50	0.9719	–	–	83.390 ± 19.71	104.60 ± 27.60	–
Tacrine	–	–	–	–	1143.312	0.9948	–	–	858.85 ± 12.11

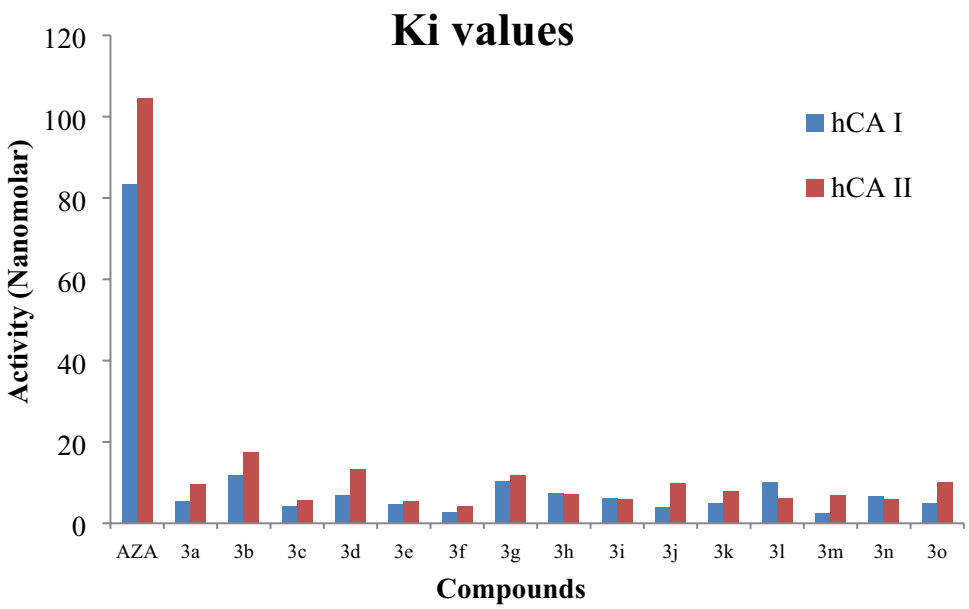


Fig. 1 K_i values of novel 4-Amino-chalcone derivatives (**3a–o**) on hCA I and hCA II

and 5. In picture 3, in the interactions between the proteins of the AChE enzyme and molecule 3d, a hydrogen bond is formed between the oxygen in the methoxy group attached to the phenyl group in molecule 3d and the TRP 5 protein. Again, pi-pi interactions occur between the phenyl group in molecule 3d and HIE 64. There is a Pi-cation interaction between the aniline ring and the LYS 170 protein. On the other hand, in the interactions between the proteins of the hCA I enzyme and the molecule 3 m, there is a pi–pi interaction between the aniline ring and the TRY 121 protein. There is a hydrogen bond interaction between the amine group in the molecule and the TRY 70 protein. However, in the interactions between the proteins of the hCA II enzyme and molecule 3f, there is a hydrogen bond between the amino group in the molecule and the HIE protein. Supplementary data for all other interactions is given in Figure S29–S72.

Molecular docking calculations were performed against enzymes of 4-amino-chalcone derivatives (**3a–o**) and biological activities of molecules were compared as a result of

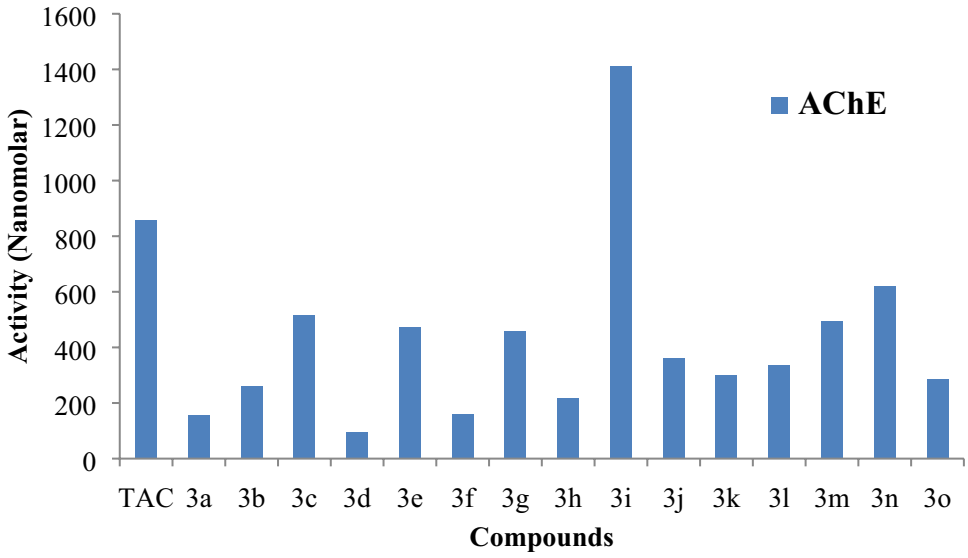


Fig. 2 K_i values of novel 4-Amino-chalcone derivatives (**3a–o**) on AChE enzymes

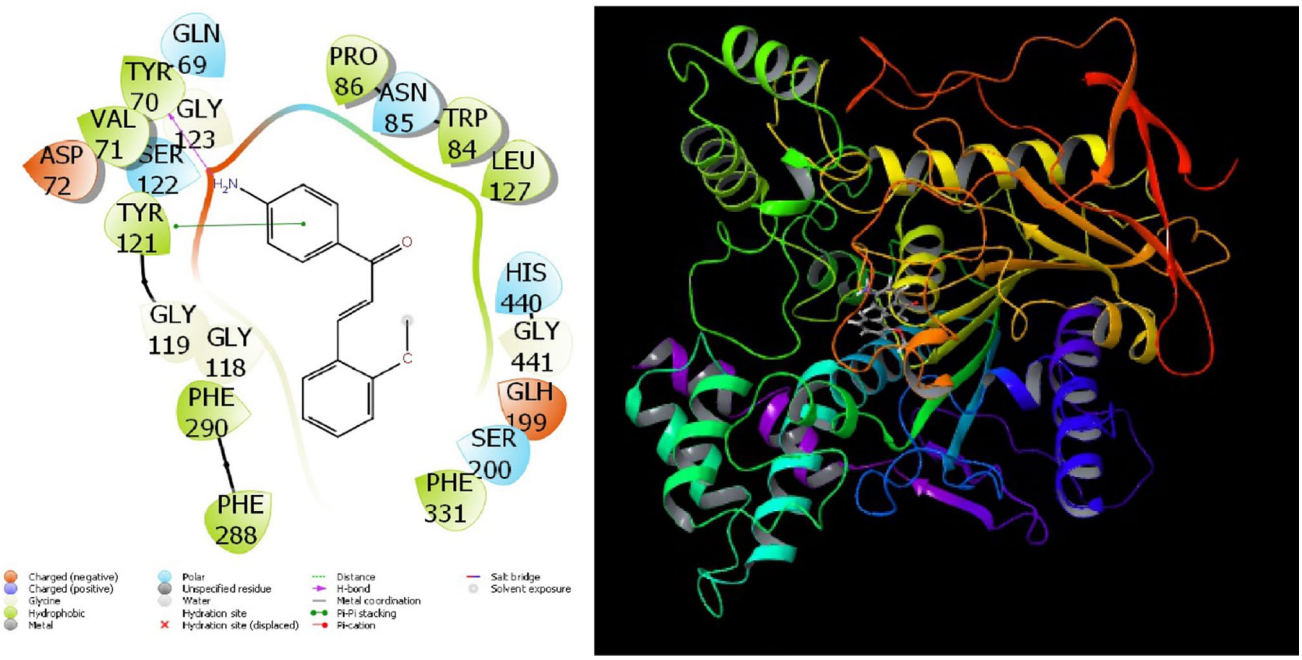


Fig. 3 Representation of interactions of molecules **3m** and hCA I enzymes

calculations. The molecular docking parameters obtained as a result of this comparison are given in Table 3 and S1.

The first parameter among parameters obtained to compare the biological activities of 4-amino-chalcone derivatives (**3a–o**) is the docking scooter. this parameter is the most important parameter to compare the biological activities of molecules. The molecular biological activity of the 4-amino-chalcone derivatives (**3a–o**) with the numerical value of the docking score parameter is the most negative. Another parameter among the parameters obtained is the Glide hbond parameter, whose numerical value gives information about the number of hydrogen bonds formed during interactions. Glide hbond parameter is affected by the atoms forming the hydrogen bond and the geometry of the hydrogen bonds. Another important parameter, that is Glide ligand efficiency parameter, is a numerical value used to sort the effectiveness of 4-amino-chalcone derivatives (**3a–o**) (Genc Bilgicli et al. 2020; Bilgiçli et al. 2020a, b). After examining the interactions of 4-amino-chalcone derivatives (**3a–o**) with enzymes, the effects and responses of these derivatives on

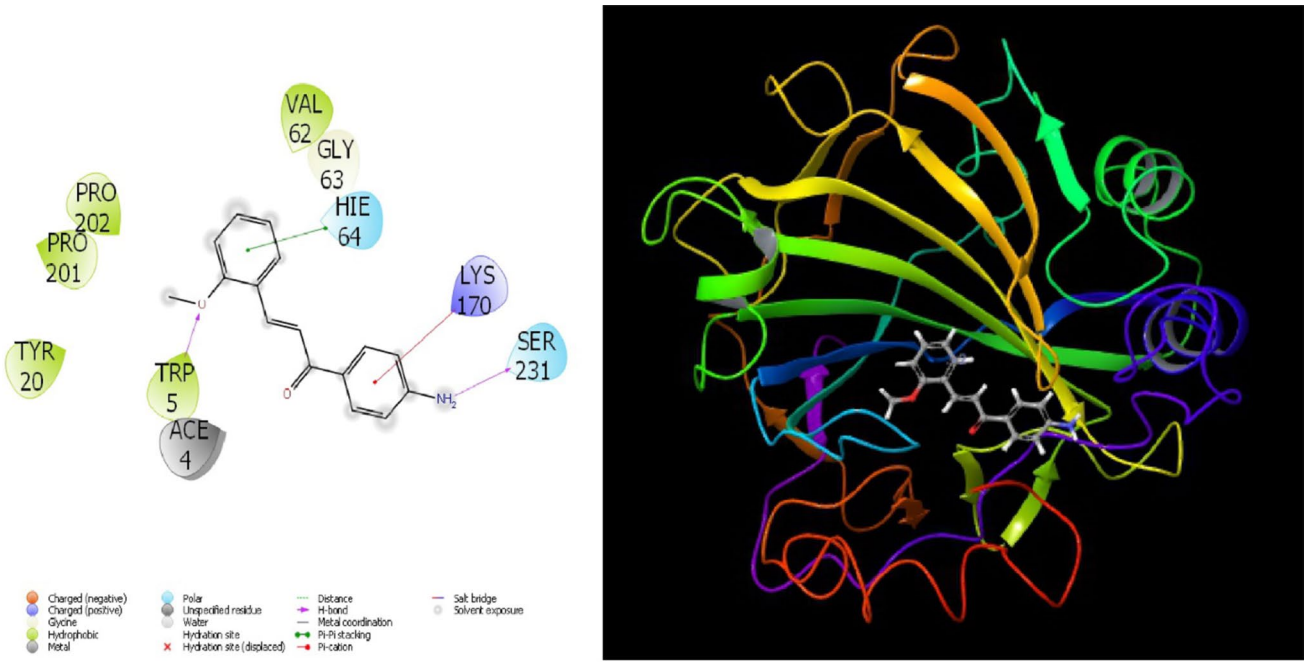


Fig. 4 Representation of interactions of molecules **3d** and AChE enzymes

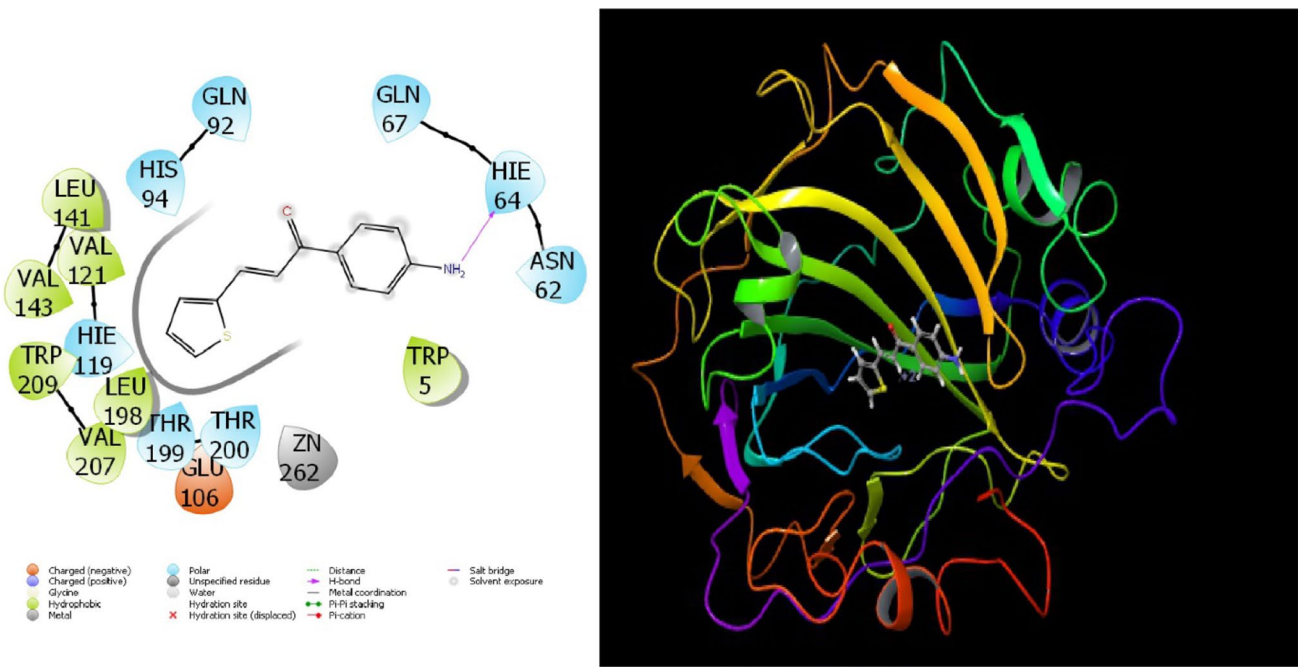


Fig. 5 Representation of interactions of molecules **3f** and hCA II enzymes

human metabolism are theoretically investigated in order to study their drug availability properties. For this, ADME/T analysis is required for 4-amino-chalcone derivatives (**3a-o**).

Each parameter obtained is as important as others to explain the drug properties of 4-amino-chalcone derivatives (**3a–o**). Because they each examined the effect or response of different organs or tissues. In particular, it should be known very well that one of the most important methods used without experiment to explain the effects and responses of 4-amino-chalcone derivatives (**3a–o**) in human metabolism

Table 3 Interaction value of studied molecule with enzymes

Molecules	Docking score		
	AChE	hCA I	hCA II
3a	− 5.22	− 4.37	− 4.43
3b	− 6.00	− 4.10	− 4.47
3c	− 3.94	− 4.28	− 4.70
3d	− 6.55	− 4.38	− 3.30
3e	− 6.26	− 3.79	− 5.40
3f	− 3.89	− 4.49	− 4.55
3g	− 6.30	− 3.88	− 4.78
3h	− 5.98	− 4.03	− 4.80
3i	− 5.80	− 3.83	− 4.99
3j	− 6.00	− 3.46	− 4.71
3k	− 6.46	− 3.80	− 4.74
3l	− 5.64	− 4.22	− 4.70
3m	− 6.07	− 3.46	− 5.65
3n	− 6.35	− 4.14	− 4.55
3o	− 5.64	− 3.80	− 4.94
AZA	–	− 3.98	− 5.19
TAC	− 6.06	–	–

is molecular docking calculations. By comparing the numerical values of these effects and reactions, it is possible to design more effective and active molecules (Taslimi et al. 2020).

As a result of the ADME/T analysis, many parameters were obtained. Some of these parameters are given in Table 4. All remaining parameters are given in table S1. The first parameter among the obtained parameters is Solute Molecular Weight, which tells how much the molecular weight of the molecule should be for human metabolism. Another parameter is Solute Hydrophobic SASA, which is the Hydrophobic component of the SASA (saturated carbon and attached hydrogen). Another parameter is QPlogHERG, which is predicted IC_{50} value for blockage of HERG K channels. Another parameter is QPPCaco, which is Predicted apparent Caco-2 cell permeability in nm/s. Caco-2 cells are a model for the gut-Blood barrier. QikProp predictions are for non-active transport. the numerical value of this parameter should be < 25 poor, > 500 great. Another parameter is QPlogBB, which is Predicted brain/Blood partition coefficient. Another parameter is QPPMDCK, which is Predicted apparent MDCK cell permeability in nm/sec. MDCK cells are considered to be a good mimic for the Blood brain barrier. QikProp predictions are for non-active transport. the numerical value of this parameter should be < 25 poor, > 500 great. Two parameters shown among the most important parameters obtained as a result of ADME/T analysis are RuleOfFive (Lipinski 2004; Lipinski et al. 1997) and RuleOfThree (Jorgensen and Duffy 2002). These parameters are more important than other parameters. When the numerical conditions of this parameter are not met, the molecule is said to not be a definite drug. RuleOfFive is Lipinski Rule of 5 and RuleOfThree is Jorgensen Rule of 3. RuleOfFive is number of violations of Lipinski's rule of five. The rules are: mol_MW < 500, QPlogPo/w < 5, donorHB ≤ 5, accptHB ≤ 10. Compounds that satisfy these rules are considered drug like (The "five" refers to the limits, which are

Table 4 ADME properties of molecules

Reference range	Solute molecular weight	QPlogHERG	QPPCaco (nm/s)	QPPMDCK (nm/s)	RuleOfFive	RuleOfThree
	130–725	(concern below − 5)	a < 25 is poor and a > 500 is great	a < 25 is poor and a > 500 is great	Maximum is 4	Maximum is 3
3a	237	− 5.56	971	479	0	0
3b	237	− 5.64	970	479	0	0
3c	237	− 5.63	970	479	0	0
3d	253	− 5.67	971	479	0	0
3e	253	− 5.57	970	479	0	0
3f	253	− 5.55	970	479	0	0
3g	258	− 5.6	971	1050	0	0
3h	258	− 5.63	970	1180	0	0
3i	258	− 5.62	970	1181	0	0
3j	302	− 5.62	971	1130	0	0
3k	302	− 5.66	970	1269	0	0
3l	302	− 5.65	970	1269	0	0
3m	229	− 5.32	969	884	0	0
3n	213	− 5.09	968	478	0	0
3o	223	− 5.68	971	479	0	0

multiples of 5.). RuleOfThree is number of violations of Jorgensen's rule of three. The three rules are: QPlogS > -5.7, QP PCaco > 22 nm / s, # Primary Metabolites < 7. Compounds with fewer violations of these rules are more likely to be orally available (Çetiner et al. 2021).

Many ADME/T parameters were calculated in the calculations. Each of the ADME/T parameters found gives information about a different property of the molecules. Molecules are desirably in the range of 130–725 g/mol. The molecular weight of the molecules is in the range of 237–258. Another parameter for molecules to become drugs is QPPCaco, which is expected to be less than 500. Of all the molecules, there are 970 units. This situation shows that the intestinal absorption of the molecules is difficult. Another parameter is QPPMDCK, the numerical value of this parameter is expected to be less than 500. but the chi of 3g, 3h, 3i, 3j, 3k, 3l, and 3m molecules is greater than 500. These drugs are not suitable for the brain.

Conclusions

Biological activities of 4-amino-chalcone derivatives (**3a–o**) against enzymes were compared. Afterwards, ADME/T analysis of this molecule was done, and it was theoretically investigated in the future. As a result of molecular docking and ADME/T calculations, the biological activities of molecules were compared against my enzyme. There is a great agreement between the experimental results and the theoretical results. However, the most important reason for some differences is that the theoretical calculations are made in an isolated environment. The results showed that 4-amino-chalcone derivatives (**3a–o**) do not have any side effects for human metabolism in the future. However, it was a good guide for future in vivo and in vitro studies. 4-Amino-chalcone derivatives (**3a–o**) had potent effects inhibiting CA enzymes such as AZA. AZA, a well-known CA receptor, is a positive regulation agent, such as topiramate, zonisamide, which methazolamide, and has been approved for epilepsy treatment and epileptic disorder.

Experimental

Measurements

General

4-Amino-chalcone derivatives (**3a–o**) were resynthesized according to published procedures (Scheme 1) (Kocyigit et al. 2018; Gürdere et al. 2020).

Enzymes studies

Determination of the effects of new compounds on acetylcholinesterase enzyme

The effect of 4-amino-chalcone derivatives (**3a–o**) used in the study on the enzyme acetylcholinesterase was investigated. In this study, Acetylcholinesterase method was used. Based on the data obtained, the inhibition types were determined by calculating the IC_{50} and K_i values. The principle of the method; As mentioned in the previous sections, AChE is used for hydrolysis of acetylcholine.

It is responsible for the formation of thiocoline and acetate, which are catalysis decomposition products. 5-thio-2-nitrobenzoic acid, a yellow compound, is formed as a result of the interaction of DTNB, which is used during inhibition studies, with thiocoline, one of the disintegration products. The color intensity of the colored compound formed is measured at 412 nm (Ellman et al. 1961). The absorbance of the sample and blind cuvettes at 412 nm at baseline and at the 5th minute is measured.

Determination of the effects of new compounds on carbonic anhydrase

Esterase activity method was used to measure the carbonic anhydrase enzyme activity. The method is based on the fact that CA has esterase activity. The principle of the method; *p*-nitrophenylasetate of the carbonic anhydrase enzyme used as a substrate. It is hydrolysis to *p*-nitrophenol or *p*-nitrophenol to give absorption at 348 nm.

In this method, both *p*-nitrophenol and *p*-nitrophenolate at 348 nm show the same absorbance. Therefore, phenol or phenolate formation does not affect the measurement during the reaction (Lineweaver and Burk 1934; Verpoorte et al. 1967; Kocyigit et al. 2017; Ökten et al. 2019). Since 348 nm *p* nitro phenyl acetate gives little absorption, it blindly.

It is used. In the measurements, an activity determination procedure was applied by mixing the reaction mixture using 3 mL quartz cuvettes.

Molecular docking method

Molecules docking is the most common method used to compare the biological activities of 4-amino-chalcone derivatives against enzymes, and there are many parameters obtained by this method (Ojha et al. 2020; Koçyiğit et al. 2020; Gezegen et al. 2020). To compare the biological activities of molecules, the numerical value of obtained many parameters that provide important information about molecules [32], is used. These parameters are used to compare the biological activities of molecules. The calculations made for this comparison consist of many stages. First, each molecule

is optimized with the Gauss software program (Frisch et al. 2009) to prepare 4-amino-chalcone derivatives for calculations. Maestro Molecular modeling platform (version 12.2) by Schrödinger, LLC (Schrodinger 2019) was used for all subsequent docking calculations.

In the next process, it is the preparation of the studied enzymes that are human acetylcholinesterase (PDB ID: 4M0E), human Carbonic Anhydrase I (PDB ID: 3LXE), human carbonic anhydrase II (PDB ID: 5AML) in this study. The protein preparation module (Schrödinger Release 2019b; Friesner et al. 2006) was used to prepare the calculations for enzymes. With this module, the water molecules in the proteins of the enzymes were removed and then the active sites of the enzymes were determined. All proteins in this active site are given freedom of movement, because in this way the proteins interact more easily with the 4-amino-chalcone derivatives. In the next step, the LigPrep module (Schrödinger Release 2019a; Sastry et al. 2013) was used to prepare 4-amino-chalcone derivatives. In the next step, calculations were made with the Glide ligand docking module (Du et al. 2020) to interact with enzyme proteins with 4-amino-chalcone derivatives. All calculations for molecular docking calculations were made using the OPLS3e method. Finally, a detailed analysis of ADME / T analysis (absorption, distribution, metabolism, excretion and toxicity) was performed for 4-amino-chalcone derivatives to be drug molecules. Many parameters were calculated using the Qikprop module (Schrödinger Release, 2020-1) of the Maestro Molecular modeling platform.

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Declarations

Conflict of interest The authors declare that there are no conflicts of interest.

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