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INHIBITION OF HUMAN PANCREATIC LIPASE BY ASPIRIN: EXPERIMENTAL AND *IN SILICO* STUDY

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Excessive accumulation of adipose tissue is a hallmark of obesity as a critical factor in the development of numerous chronic medical problems. Pancreatic lipase (PLase), which controls the absorption of fats in the intestine, has gained significance as a target in anti-obesity therapy. This study aimed to evaluate the potential effects of Aspirin as a PLase inhibitor and a weight-loss agent compared to the commonly used anti-obesity drug Xenical. Pancreatic lipase was purified 28.5-fold from the plasma of obese male volunteers using ion-exchange chromatography. Enzyme activity was evaluated using p-nitrophenyl butyrate as a substrate. The kinetic analysis of Aspirin effect on purified enzyme activity revealed a competitive inhibition mechanism with K_i of 24.3 mM. In vivo studies were performed using 20 male Wistar rats randomly divided into four equal groups provided with: 1 – control conditions; 2 – high-fat diet (HFD) for 12 weeks; 3 – HFD and Xenical orally (10 mg/kg BW daily); 4 – HFD and Aspirin orally (14.4 mg/kg BW daily). In an HFD group, increased animals body weight and elevated PLase activity in plasma compared to the control were demonstrated. Treatment with both Aspirin and Xenical resulted in a significant decrease in body weight and PLase activity compared with untreated HFD rats. Molecular docking of Human Pancreatic lipase-related protein 1 (PDB ID: 2PPL) binding with Aspirin and Xenical showed the values of binding energy (ΔG) 5.4 and -4.4 kcal/mol, respectively, indicating a stronger protein interaction with Aspirin compared to Xenical. This combined study reinforces the conclusion that Aspirin has the potential to be a novel anti-obesity agent.

K e y w o r d s: obesity, pancreatic lipase, Aspirin, Xenical, kinetic inhibition analysis, anti-obesity effect, human pancreatic lipase-related protein 1, in silico study.

Obesity is recognized as the problem with the greatest rate of growth in industrialized and developing countries, and it is associated with high rates of morbidity and mortality. It is a major threat to the world's health [1]. As a result, the number of chronic metabolic disorders caused by fats increases [2]. Several chronic disorders, including diabetes [3], hyperlipemia, hypertension [4], and cardiovascular disease [5], are intimately linked to obesity, which is also a significant risk factor for these conditions [6]. Many fundamental processes have been examined for treating obesity; nevertheless, these processes entail significant drawbacks. Pancreatic lipase (PL) (EC 3.1.1.3), the primary lipolytic enzyme released by the pancreas, has gained significance as an obesity target in recent years [1, 7]. It is an important digestive enzyme that catalyzes the breakdown of triacylglycerol into monoglycerides and free fatty acids (Fig. 1) [8]. This enzyme is in charge of the body's absorption of fat, which causes obesity as a chronic metabolic condition [9]. Through the whole breakdown of dietary fat, PL is an essential enzyme in fat absorption [10, 11].

Pancreatic lipase inhibition is the most widely studied mechanism for identifying potential anti-obesity agents. If the lipase enzyme is inhibited, free fatty acid and total cholesterol levels decrease [12]. Several synthetic medications have entered the market, but they have not significantly impacted obesity management. One promising and relatively safe approach to developing anti-obesity drugs is to modify lipid metabolism by using PL to block dietary fat absorption [13]. The only commonly used drug approved for long-term use is Xenical, which was designed and developed as an anti-obesity medication. It inhibits intestinal lipase activity, reducing dietary fat absorption [14]. Rhodanine-3-acetic acid derivatives have been synthesized and used for PL inhi-

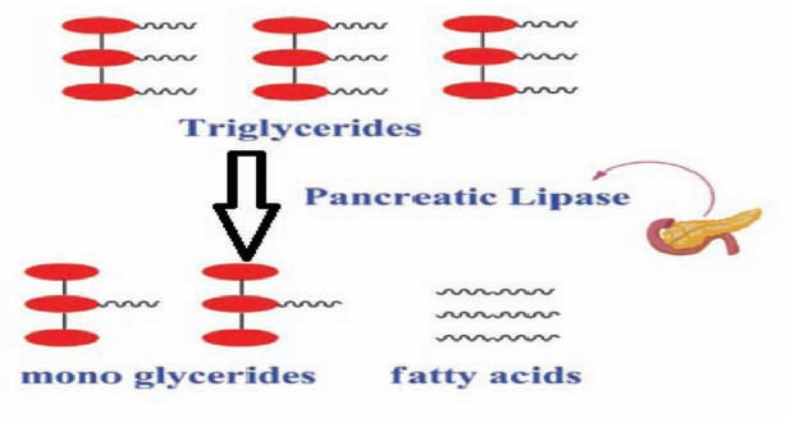

Fig. 1. Schematic representation of pancreatic lipase action

bition [15]. *In vitro,* synthesized aurone derivatives such as 4,6-dihydroxyacetone, 6-hydroxyaurone, 4,6-dialkoxyaurone, and 6-alkoxyaurone inhibited PL. The inhibitory effect was spectrophotometrically measured and compared to Xenical [16]. Successful drug discovery and development can be supported by computer-aided techniques, such as structure-based simulation with docking software, which are highly useful in identifying new compounds for effective targets [17]. This study aims to investigate the potential use of aspirin as a weight-loss drug by purifying pancreatic lipase from the blood plasma of obese humans to assess its inhibitory kinetics. It involves bioassays in obese Wistar rats fed a high-fat diet to monitor changes in weight and enzyme activity compared to Xenical, complemented by molecular docking simulations to assess aspirin's binding to human pancreatic lipase.

Materials and Methods

Chemicals. Bovine serum albumin, ammonium sulfate, and p-nitrophenyl butyrate (p-NPB) were purchased from Merck. Diethylaminoethyl cellulose and copper sulfate were bought from Sigma-Aldrich. Aspirin and Xenical medicines were purchased from a pharmacy, manufactured by Bayer and Roche, respectively.

Collection of human blood. The study involved nine obese male volunteers free from any disease in Mosul, Iraq. Five milliliters of blood were collected from each person and placed in a tube containing ethylenediaminetetraacetic acid, with stirring to prevent clotting. The blood was centrifuged at 1500 xg for 10 min using a refrigerator centrifuge at 4°C. After that, the plasma was obtained and preserved for subsequent experiments.

Determination of protein. The Biuret method [18] measured the total protein concentration at 540 nm. Using bovine serum albumin as the reference, a calibration curve was created.

Pancreatic lipase assay. The Lee et al. [19] method was used to assess pancreatic lipase activity. The enzyme catalyzes p-NPB hydrolysis. The p-nitrophenol that was generated was detected at 405 nm.

Purification of Pancreatic Lipase. Dialysis. The final enzyme from the preceding step was placed in a dialysis tube. A buffer change was made six times while the tube was being stirred against phosphate buffer (10 mM, pH 7.2) at 4°C.

Ion exchange chromatography. A column containing DEAE-Cellulose (25×2.5 cm) was loaded with the dialyzed solution, and then a 10 mM phosphate buffer (pH 7.2) was added. A flow rate of 1 ml per minute was used to elute the protein. By following the absorbance at 280 nm, the protein was found. After determining the fractions' lipase activity, they were gathered and lyophilized for use later in inhibitory studies [20, 21].

Preparation of inhibitors*:* the stock solutions of aspirin were prepared at 1 M.

Lipase inhibition. Purified enzyme activity was inhibited by incubating it with Aspirin at 25°C for 15 min. The activity was determined at 405nm. The inhibition modes were tested via a Lineweaver-Burk plot using substrate concentrations from 0.5-3 mM.

The percentage of PL inhibition (I%) was calculated using the following equation:

$$I\% = [(\Delta A_o - \Delta A)/\Delta A_o] \times 100.$$

Here, ΔA_o denotes the absorbance variance between a blank and the control, where ΔA denotes the

absorbance variation of the sample and the blank, and Ao denotes the absorbance of the control.

Anti - obesity effect of aspirin in rats as evidence of in vivo inhibition of human pancreatic lipase. Preparation of high-fat diet. The process outlined by Smine (2017) [22] was followed in preparing the high-fat diet (HFD). The typical foods already saturated with liquefied lamb fat make up the HFD. After heating this fat to 100°C to liquefy it, the plugs were submerged in the hot fat for 15 min. After cooling at room temperature, the HFD food was given.

Animals and experimental protocol design. Male Wistar rats weighing 190–210 g were purchased from the International Animal Care and Use Committee, College of Veterinary Medicine, University of Mosul. Rats were housed in a typical pet shop with easy access to water and food, at 23 ± 0.5°C and a 12-hour light/dark cycle. After two weeks of acclimation, the rats were randomly divided into four equal groups, each containing five rats, and each group received the following treatment [23]: Group 1 – Provided a typical laboratory food and unlimited access to water, as a control. Group 2 – Provided with HFD for 12 weeks to induce hyperlipidemia. Group 3 – The HFD and Xenical (10 mg/kg BW daily) are provided. Group 4 – The HFD and Aspirin (14.4 mg/kg BW daily) are provided.

For twelve consecutive weeks, Xenical and Aspirin were given orally. An earlier study was used to determine the Xenical dosage [24]. According to initial experience, this dose (14.4 mg/kg BW, orally) has been quite helpful for determining dosage. Before administration, the experimental individuals were freshly prepared, and the most current recorded body weight was used to determine the administration protocol.

Measurement of body. A digital balance scale was used to weigh each rat's body weight, which was noted on Day 0 and every week throughout the experiment. The variance between the starting and end body weight was used to calculate the weight difference [25].

Collection of rats' blood. When the experiment periods concluded, all of the rats were decapitated after fasting for 12 h continuously. Centrifuging the blood at 1500 xg for 10 min at 4°C was performed immediately after collection [26]. The resulting plasma had been separated, kept at -80°C until required for measuring PL activity.

Molecular docking study. Molecular docking studies were conducted with the AutoDock Vina 1.1.2 software. The 3D structure of Human Pancreatic lipase-related protein 1 (PDB ID: 2PPL) and its structure, attained at a resolution of 2.2 angstroms, was introduced by the RCSB Protein Data Bank (https://www.rcsb.org). All molecules of water and a ligand have been eliminated prior to a docking calculation for the compound studied. The ChemAxon Marvin Sketch 5.3.735 software was used to generate the ligand and conformation 3D structures, which were then saved in the Mol 2 format [27]. Using Gaussian 09, the ligand structures were optimized and their energy was minimized. Using Auto Dock Tools (ADT) 1.5.6, the protein and ligand were prepared. By simulating the interactions between the protein and the chemical, the binding affinities of Aspirin with Human Pancreatic lipase-related protein 1 have been determined. A flexible docking mode, automatically created to validate each ligand, was used to carry out the docking procedure. Discovery Studio Visualizer (BIOVIA, Discovery Studio, v4.0.100.13345) was employed to observe the ligand's and targeted proteins' interactions [28].

Statistical analysis. The standard error of the mean (mean ± SEM) was used to express all of the values. Using SAS software version 9.3, Duncan's test compared the means. At $P \leq 0.05$, these variations appeared to be statistically significant.

Results and Discussion

Lipase purification. The data in Table 1 illustrate that after the dialysis process, the specific activity became 2.86 U/mg protein compared to the crude enzyme with a purification fold of 2.15. The dialyzed enzyme was run through the DEAE-Cellulose column, and we obtained a single isoenzyme (Fig. 2) with a specific activity value of 37.95 U/mg protein and a purification fold of 28.53.

Lipases are present in most animal tissues. In mammals, neutral fats are digested by two main enzymes: gastric lipase and PL [29]. Purification and characterization of lipases are based on their activity and stability relative to temperature and pH [30]. A single peak of lipase was obtained from human pancreatic juice by using a cation exchange resin [31]. Lipase was isolated from the porcine pancreas and found to have a single protein chain with a molecular mass of approximately 50 kDa [32]. Most other studies regarding the inhibition of this enzyme had been based on the use of porcine pancreatic lipase due to its availability in the marketplace. However, this particular study stands out in that it isolated this lipase

Table 1. Purification steps of PL from obese human plasma

Purification steps	Total volume, ml	Total protein, mg	Total activity, U*	Specific activity, (U/mg)×10^{-3}	Yield, %	Purification fold
Crude	11.4	702.2	0.934	1.33	100	–
Dialysis	11.9	519.2	1.485	2.86	159	2.15
Ion exchange	37.6	51.8	1.966	37.95	210.49	28.53

Note. *U – unit refers to an amount of lipase that releases a micromole of p-nitrophenol/min

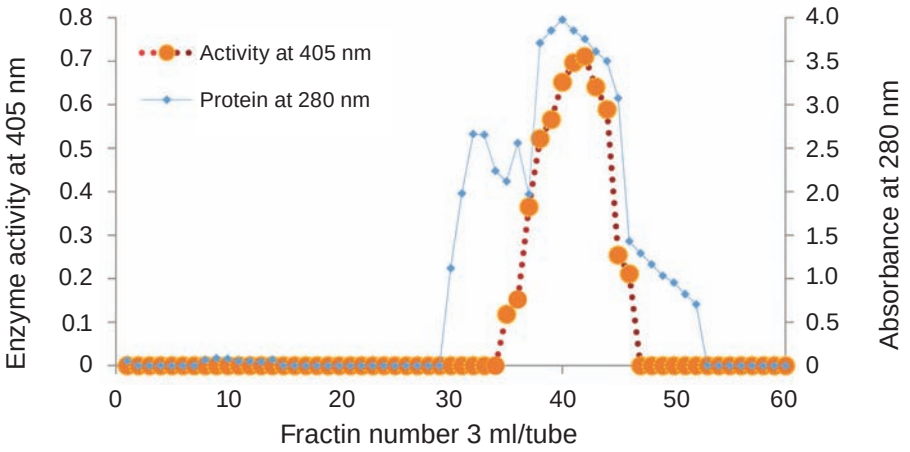

Fig. 2. Partial purification of lipase by DEAE-Cellulose chromatography

from the blood plasma of people who suffer from obesity. The biologically derived lipase plays an extremely significant role in ensuring that this study's results are much more clinically significant than other studies that utilize pig-based lipase or other lipases derived from animals. The PPL lipase is extremely similar to lipase found in humans, coming in at about 85%. It is, however, not an exact match and has some differences.

The effect of Aspirin on the PL activity. Table 2 shows the inhibitory effect of purified PL activity using different Aspirin concentrations. It was noted that with increasing concentration of the inhibitor, the inhibitory effect increased and reached a maximum of 81.25% at 40 mM. The value of IC_{50} was calculated by the equation: $IC_{50} = 50\text{-}b/a$ by using the equation of the straight line, where *a* and *b* represent the slope and intercept values, respectively, and was found to be 22.18 mM.

Mode of inhibition. The purified PL activity was tested for inhibition in the presence of 22.18 mM of Aspirin as an inhibitor by drawing a Lineweaver-Burk plot. According to the findings, competitive inhibition was noted (Fig. 3). K_m increased from 2.12 to 4.7 mM; however, V_{max} was established and found to be stable at 0.101 U/ml. The inhibition constant was calculated and found to be 24.35 mM.

Aspirin is one of the most significant pharmaceutical successes in the world of the last century. The role of Aspirin in avoiding cardiovascular and cerebrovascular diseases is revolutionary. The discovery that Aspirin inhibited prostacyclin synthesis paved the way for future nonsteroidal anti-inflammatory drugs and other cyclooxygenase (COX) inhibi-

Table 2. Aspirin effect on the activity of pancreatic lipase

Aspirin, mM	5	10	15	20	25	30	35	40	45
Inhibitory effect, %	19.68	29.56	31.77	49.56	47.84	55.61	79.56	86.25	100

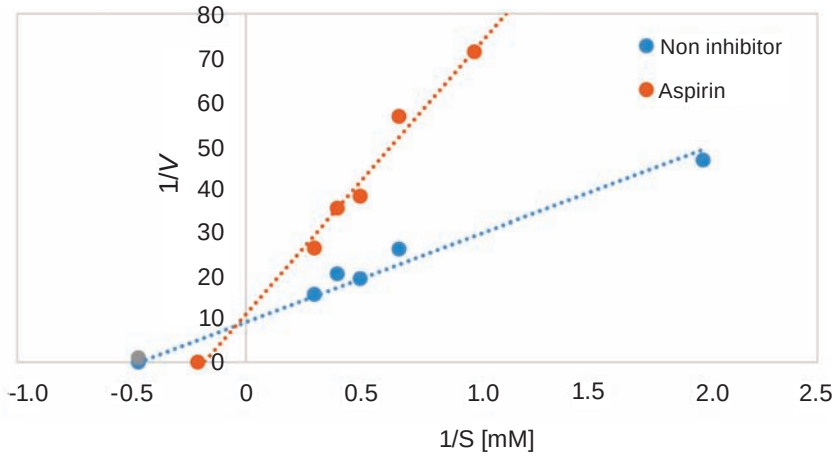

Fig. 3. Inhibition mode of purified lipase by Aspirin

tors to be developed [33]. A reason for this type of inhibition may be that Aspirin has a structure similar to that of the substrate, which is represented by the fact that it contains an ester group that the lipase enzyme breaks down.

PL was inhibited competitively by carnosic acid with a K_i of 5.4 µg/ml [34] and the saponin, platycodin, with a K_i of 0.18 mM [35]. However, a polyphenol, Licochalcone was demonstrated to inhibit PL at 35 µg/ml reversibly and non-competitively with the K_i value of 11.2 µg/ ml based on a Lineweaver–Burk plot analysis [36]. *In vitro,* PL activity was inhibited by epicatechin, cyanidin, peonidin, and petunidin at 1.25–100 µg/ml. It was noted that the inhibition mechanism for all these compounds was uncompetitive [37].

Effect of Xenical and Aspirin on body weight. The Wistar rats became the model for investigating aspirin's *in vivo* anti-hyperlipidemic and anti-obesity action, simultaneously comparing its potency with Xenical, a clinically recognized inhibitor of PL. The animal model becomes indispensable when developing a biological model which would mimics human obesity and hyperlipidemia. Such processes cannot be fully modeled using *in vitro* systems or *in silico.* Moreover, changes in body weight, pancreatic lipase activity, and appropriate dosage of the active agent depend upon absorption, distribution, and metabolism within a healthy organism; such changes can be studied only *in vivo.* Thus, two complementary approaches are combined in this study.

Drawing representative curves of BW evolution was made possible by closely monitoring the evolution of BW in each of the four groups of rats for a full 12-week period. Our findings demonstrate that between the first and the last day, the HFD diet significantly increases the animals' body weight (Fig. 4). BW grew in rats eating the HFD diet from 207.12 ± 2.36 to 411.70 ± 5.33 g compared to control rats from 195.54 ± 4.37 to 308.86 ± 3.94 g.

In comparison to the HFD control group, treatment with Xenical and Aspirin significantly decreased body weight. BW reduced from 201 ± 2.91 to 331.3 ± 9.62 g and from 205 ± 2.08 to 367 ± 10.22, respectively. This proves that whereas regular ingestion of HFD causes obesity and related problems, regular ingestion of usual food has no detrimental consequences on animal health. The BW is correlated with the makeup of the meal, not the quantity of food. Total body weight and plasma pancreatic lipase activity in the study spanned 12 weeks, thereby filling the gap that exists between the results obtained from the laboratory study, as lipase inhibition, to actual weight regulation in the body.

Effect of aspirin on PL activity in rats. Several doses of aspirin were first administered to healthy rats to identify the most effective dose for suppressing pancreatic lipase activity before applying this dose to high-fat-diet (HFD)–induced obese rats. The dose–response relationships and physiological mechanisms of action can be determined only through whole-organism studies. These animal experiments, therefore, provided crucial *in vivo* evidence in support of the earlier *in vitro* findings that showed aspirin inhibits human pancreatic lipase. Table 3 shows the determination of the most effective dose of aspirin in reducing lipase activity levels in healthy rats. The effective dose value is 14.4 mg/kg BW. It was noted that the lipase activity decreased significantly to 0.223 ± 0.012 at

Table 3. Effect of aspirin doses on PL activity in rats. Values are expressed as means ± s.e. (n = 5)

Dose of Aspirin, mg/kg BW	Control	3.6	7.2	10.8	14.4	18
PL activity, U/ml	0.371±0.064[a]	0.365±0.047[a]	0.347±0.073[a]	0.296±0.055[b]	0.223 ±0.012[c]	0.283±0.043[b]

Note. Significant differences are indicated by superscript characters between groupings horizontally. Significant differences exist between values that do not share the same letter ($P \leq 0.05$)

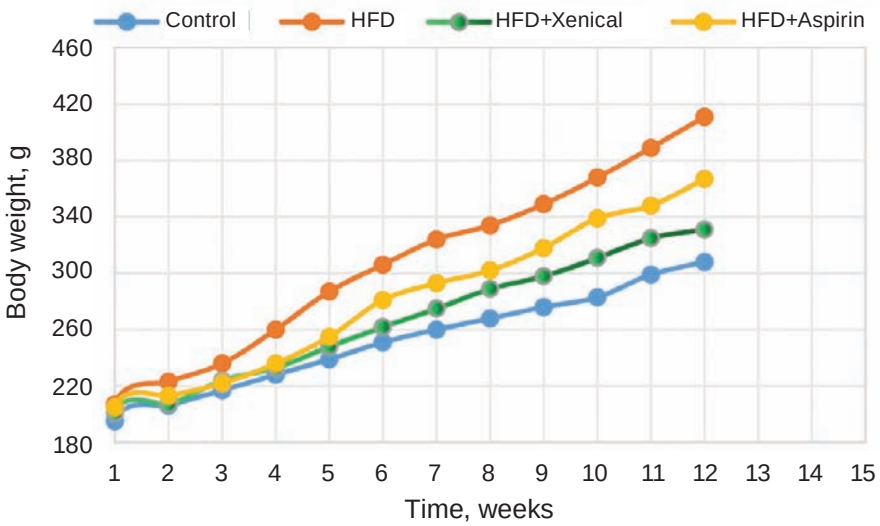

Fig. 4. Effects of Xenical and Aspirin on body weights

this dose compared to the control group, which was 0.371 ± 0.064.

High-fat diet treatment significantly increased lipase activity by 0.545 ± 0.097 U/ ml, compared to the control group, 0.312 ± 0.083 U/ml. On the other hand, the lipase activity was significantly decreased to 0.415 ± 0.057 and 0.458 ± 0.044 when treated with Xenical and Aspirin, respectively, compared with the high-fat diet rats group (Table 4). Knowing that the effect of the drug Xenical was greater than that of the drug Aspirin.

Molecular docking study. Molecular docking results revealed the binding modes of Aspirin with Human pancreatic lipase-related protein 1. Fig. 5 (*A-C*) illustrates the formation of the Aspirin ligand-protein complex in the active site of PL (ID: 2PPL), with a ΔG binding energy value of -4.7 kcal/mol. The formed complex was stabilized by six hydrogen bonds (shown by green dotted lines) with four amino acids, ASP A:215, GLY A:181, LEU A:187, and THR A:184. Different colored dotted lines show various types of bonding interactions (like alkyl with PRO A:274, Van der Waals, and Donor-Donor).

On the other hand, Fig. 6 (*A-C*) shows the creation of a compound (Xenical) ligand-protein complex in the active site of pancreatic lipase enzyme (ID: 2PPL) with a ΔG binding energy value of -5.4 kcal/mol. The formed complex was stabi-

Table 4. Effects of Aspirin (14.4 mg/kg) BW on PL activity of rats. Values are expressed as means ± s.e. (n = 5)

Rat groups	Control	HFD	HFD + Xenical	HFD + Aspirin
PL activity, U/ml	0.312±0.083[c]	0.545 ±0.097[a]	0.415±0.057[b]	0.458 ±0.044[b]

Note. Significant differences are indicated by superscript characters between groupings horizontally. Significant differences exist between values that do not share the same letter ($P \leq 0.05$)

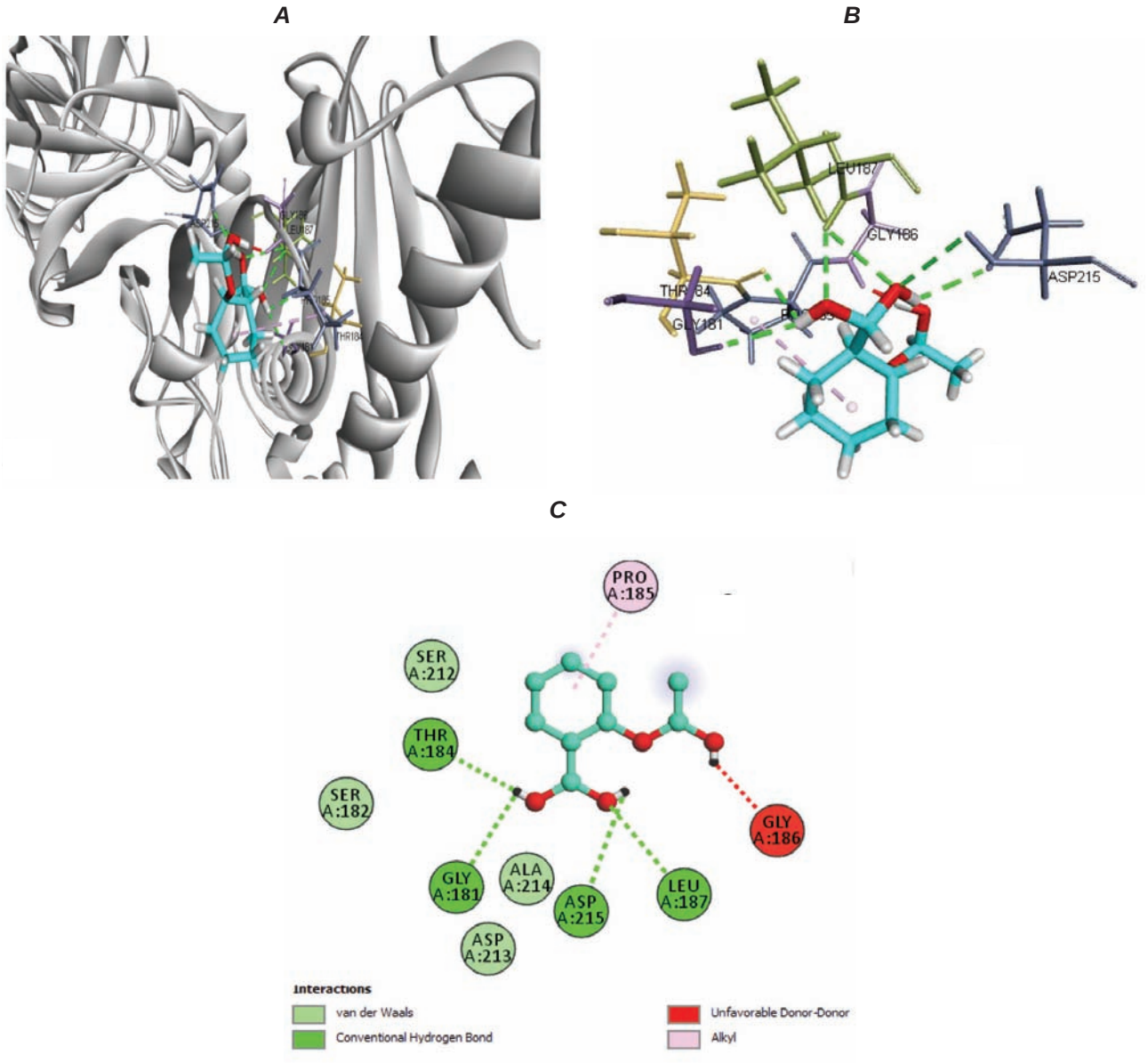

*Fig. 5 (**A**) illustrates the interactions between the pancreatic lipase enzyme (ID: 2PPL) in a 3D ribbon form and aspirin, shown in a stick model with amino acids of the enzyme (ID: 2PPL). (**B**) depicts specific amino acid residue interactions with Aspirin in a 3D model. (**C**) shows 2D interactions of aspirin with specific amino acids*

lized by five hydrogen bonds (shown by green dotted lines) with four amino acids, GLN A:146, 146, LEU A:72, 72, and SER A:73. Along two types of bonding interactions (like alkyl with ARGA A:55, ILE A:69, PRO A:49, and Van der Waals) are shown by different color dotted lines.

Several molecular docking studies have been conducted in this regard. For instance, epicatechin, cyanidin, and peonidin exhibited strong binding energy with − 7.529 to − 6.941 kcal/mol against 2PPL protein. The strongest binding was shown to Glu102, Ser 129, Ile 97, and Trp 270 [37]. Through van der Waals forces, flavonoid derivatives interacted with certain residues at the binding site, especially Gly 76, Ile 78, Tyr 114, Leu 153, Ala 178, Phe 215, His 263, and Leu 264. Additionally, four hydrogen bonds were created with crucial residues: Ser 152, Phe 77, Asp 79, and Arg 256 [38]. On the other hand, acteoside, a major active component of Chinese tea, has shown inhibition of PL. The docking results sustained the hydrogen bonding of acteoside with Lys 271, Leu 272, and Thr 68 of an enzyme,

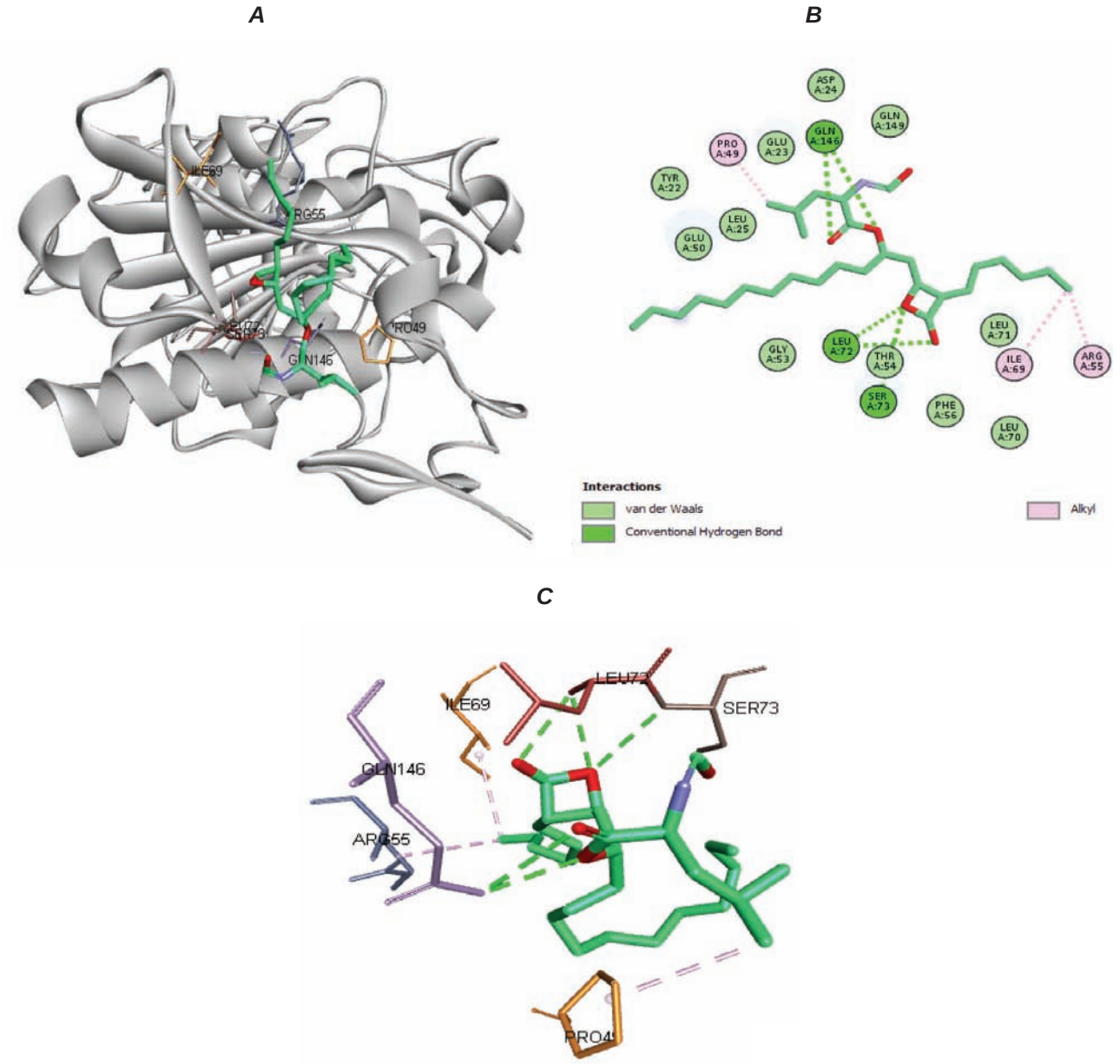

*Fig. 6. (**A**) illustrates the interactions between the pancreatic lipase enzyme (ID: 2PPL) in a 3D ribbon form and Xenical, shown in a stick model with amino acids of the enzyme (ID: 2PPL). (**B**) depicts specific amino acid residue interactions with Xenical in a 3D model. (**C**) shows 2D interactions of Xenical with specific amino acids of the enzyme*

which declines catalytic activity [39]. Remarkably, Gly 76, Phe 77, Ile 78, Asp 79, and Phe 215 are residues placed in the lid domain, while Ser 152 is a vital amino acid within the catalytic triad (Ser 152-Asp 176-His 263) on the enzyme [40]. According to the investigation, Xenical exhibits reversible covalent inhibition at the active site Ser 152, and its hydrophobic chains bind to residues in the lid domain, specifically Gly 76 to Phe 80 and Leu 213 to Met 217 of PL [41].

Simulation and imaging of the molecular interaction between aspirin and human pancreatic lipase binding protein 1 (PPL-ID: 2PPL), and determination of the binding energy, support the experimental data by providing experimental affirmation of binding affinity, because they directly visualize the binding process of both Xenical and aspirin occupying the active site of the targeted enzyme.

Conclusion. Obesity is a serious global public health issue that is worryingly becoming worse

every day, and reducing energy intake through methods that work via intestinal absorption. Therefore, pancreatic lipase (PL) is an enzyme that hydrolyzes dietary triglycerides consumed through meals. The strategy commonly used in PL inhibitors is based on the structure of the natural substrate of lipase. Compared to Xenical, Aspirin showed antihyperlipidemic action and an inhibitory effect on the pancreatic lipase activity *in vivo* using Wistar rats. PL was purified and then inhibited *in vitro* by Aspirin. The kinetics data revealed a competitive inhibition with a K_i of 24.35 mM. As a complementary study and to discover the interactions between this inhibitor and Human Pancreatic lipase-related protein 1 (PDB ID: 2PPL), *in silico* analysis was conducted. Aspirin-protein complexes at the active site of (ID: 2PPL) had a binding energy value ΔG of -4.7 kcal/mol. However, the binding energy value of Xenical-protein complexes was -5.4 kcal/mol. It is important to understand that several parameters, including the particular binding site and method of interaction, greatly influence the pharmacological effects of a chemical. This combined strategy reinforces the conclusion that aspirin has the potential to be a novel anti-obesity agent.

Conflict of interest. The authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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ІНГІБУВАННЯ ЛІПАЗИ ПІДШЛУНКОВОЇ ЗАЛОЗИ ЛЮДИНИ АСПІРИНОМ: *IN SILICO* ДОСЛІДЖЕННЯ

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Надмірне накопичення жирової тканини є характерною ознакою ожиріння та критичним фактором у розвитку численних медичних проблем. Панкреатична ліпаза (PLase), яка контролює всмоктування жирів у кишківнику, стала важливим таргетним об'єктом у терапії проти ожиріння. Метою цього дослідження було оцінити потенційні ефекти аспірину як інгібітора PLase та засобу для схуднення у порівнянні з широко використовуваним препаратом проти ожиріння Xenical. Панкреатичну ліпазу із плазми крові чоловіків-добровольців із ожирінням було очищено у 28,5 раза за допомогою іонообмінної хроматографії. Активність ензиму оцінювали з використанням р-нітрофенілбутирату як субстрату. Кінетичний аналіз дії аспірину на активність очищеного ензиму показав механізм конкурентного інгібування з K_i 24,3 мМ. Дослідження *in vivo* проводили на 20 самцях щурів лінії Wistar, рандомно розділених на чотири рівні групи: 1 – контроль; 2 – отримували дієту з високим вмістом жирів (HFD) протягом 12 тижнів; 3 – HFD та пероральний прийом ксенікалу (10 мг/кг маси тіла щодня); 4 – HFD та пероральний прийом аспірину (14,4 мг/кг маси тіла щодня). У групі HFD спостерігали збільшення маси тіла та підвищену активність PLase у плазмі порівняно з контролем. Терапія аспірином та ксенікалом призвела до значного зниження маси тіла та активності PLase порівняно з щурами HFD, які не отримували аспірин чи ксенікал. Молекулярний докінг зв'язування протеїну 1, панкреатичної ліпази людини (PDB ID: 2PPL), виявило значення енергії зв'язування (ΔG) 5,4 та -4,4 ккал/моль, відповідно, що вказує на більш сильну взаємодію протеїну з аспірином порівняно з ксенікалом. Це комбіноване дослідження підтверджує висновок, що аспірин має перспективи стати новим засобом проти ожиріння.

Ключові слова: ожиріння, панкреатична ліпаза, аспірин, ксенікал, аналіз кінетичного інгібування, ефект проти ожиріння, протеїн 1 панкреатичної ліпази людини, *in silico* дослідження.

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