An In-Silico Approach to Evaluate Bioactive Molecules of Aloe Vera Leaf Extracts in Inhibiting the Glycogen Synthase Kinase-3β (GSK3-β) Protein for Faster Diabetic Wound Healing Potential

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Abstract: A complex web of dynamic systems is involved in the wound healing of excisional skin injuries, which poses a significant therapeutic challenge. Skin graft transplantation and wound dressings are among the several methods that have been suggested in order to preserve the essential structure and function of the damaged tissue. GSK3-β, which is a main target to accelerate the healing process of wounds, is a signaling route that is part of the PI3K/AKT pathway, which is activated phosphatidylinositol 3 kinase/protein kinase B pathway. The efficient use of natural products in wound care has been the subject of extensive research in recent years. Natural products offer a multi-targeted strategy, particularly in treating chronic wounds, because they include many phytoconstituents that may work on different phases of wound healing. The effectiveness of the main compounds found in aloe vera leaf extracts as wound-healing agents against GSK3-β was evaluated in this work using in-silico techniques. Compared to the co-crystallized ligand (-6.2 kcal/mol), aloenin 2'-p-coumaroyl ester showed high docking scores (-9.5 kcal/mol) and robust binding to the GSK3-β protein. The docking properties of Aloenin 2'-p-coumaroyl ester and the outcomes of molecular QSAR might be further utilized to develop a GSK3-β inhibitor.

Keywords: aloe vera; diabetic wound healing; GSK-3β; in-silico; QSAR; docking.

1. Introduction

Diabetes mellitus (DM) is a medical syndrome that causes abnormal glucose, protein, lipid, and electrolysis metabolism levels. These abnormalities are chronic and metabolic in nature, and they lead to a lack of control over blood glucose levels [1]. Diabetes mellitus (DM) is a critical illness that ranks eighth on the global disease list. DM caused up to 1.4 million (2.6%) fatalities globally in 2011 and 1 million (1.9%) deaths in 2000 [2]. According to the American Diabetes Association (ADA), four subtypes of diabetes mellitus can be classified clinically: type 1 DM (T1DM), formerly known as insulin-dependent DM (IDDM) or juvenile-onset DM, primarily caused by pancreatic β-cell destruction and diagnosed as absolute insulin deficiency; type 2 DM (T2DM), formerly known as noninsulin-dependent DM (NIDDM) or adult-onset DM, primarily characterized by insulin resistance with relative insulin deficiency

or secretory defect with insulin resistance; gestational DM (GDM), in which women are diagnosed with diabetes during pregnancy; and other distinct types of diabetes that were not included in any previous forms [3].

According to estimates, 2.8% of people worldwide were anticipated to have diabetes in 2000. By 2030, that number is predicted to rise to about 4.4% [3]. By 2030, 366 million people will die from diabetes-related causes of mortality [4]. According to predictions from the World Health Organisation (WHO), 415 million people worldwide will have diabetes in 2015; by 2040, that number is predicted to increase to 642 million [5]. There is a noticeable rise in the number of diabetes patients between 45 and 64 in several countries, especially in China, India, and Southeast Asia [6]. Diabetic foot ulcers, also known as diabetic wounds, are the most frequent consequence of this condition, leading to significant financial and medical issues [7,8]. Several factors, including insufficient tissue perfusion, inhibition of re-epithelialization, low collagen synthesis, peripheral neuropathy, altered red blood cell rheology, and weakened host immunity, can result in non-healing ulcers on the legs and feet, which are common and severe side effects of diabetes [9]. Diabetes is known to impede effective reparative processes, leading to the production of chronic wounds that do not heal, regardless of the exact etiological cause [8].

GSK3-β, which is a primary target to accelerate the healing process of wounds, is involved in the PI3K/AKT system, also known as the Activated Phosphatidylinositol 3 Kinase/Protein Kinase B signaling pathway [7]. This target protein has a role in migration, metabolism, and cellular inflammation. Numerous investigations have demonstrated that the PI3K/AKT pathway-mediated phosphorylation of the Ser9 site results in the downregulation of GSK3-β protein, which is necessary for the healing of chronic wounds [10]. It has been discovered that phosphorylated protein promotes migration, decreases apoptosis, and increases collagen synthesis [7].

There are many different species of succulent plants in the Liliaceae family, which includes the Aloe genus. The most significant is aloe vera, a decorative and healing plant. It may be found in Africa, Asia, and the Mediterranean regions of Southern Europe. This essence is dispersed worldwide, particularly in arid locations for the original plant [11]. Aloe vera exhibited a range of biological and pharmacological properties, such as anti-inflammatory [12], immuno-stimulatory [13], cell growth stimulatory [14], anti-viral [15], antibacterial [16], anti-fungal [17], and anti-atherosis [18]. Rather than coming from a single component, the biological actions of aloe vera leaves may be caused by the compounds' propensity to work in concert [11]. This work used an in-silico technique to predict the diabetic wound healing agents using six bioactive chemicals (Figure 1) discovered in Aloe vera leaves. Additionally, the reference chemical in this investigation was sulphathiazole. Ahamed et al. reported that after administering sulphathiazole, the mice exhibited enhanced collagenation and reduced macrophage accumulation at the site of damage. In animals treated with sulphathiazole, the epithelialization was complete by the eighteenth day following wounding, with 969.4% of the wounds contracting. The rats administered with sulphathiazole exhibited a noteworthy rise in the incision wound's tensile strength (582.04 ± 4.05 g). Moreover, sulphathiazole demonstrated a hydrogen bond with the Asp200 residue in the GSK-3β protein's active site [19].
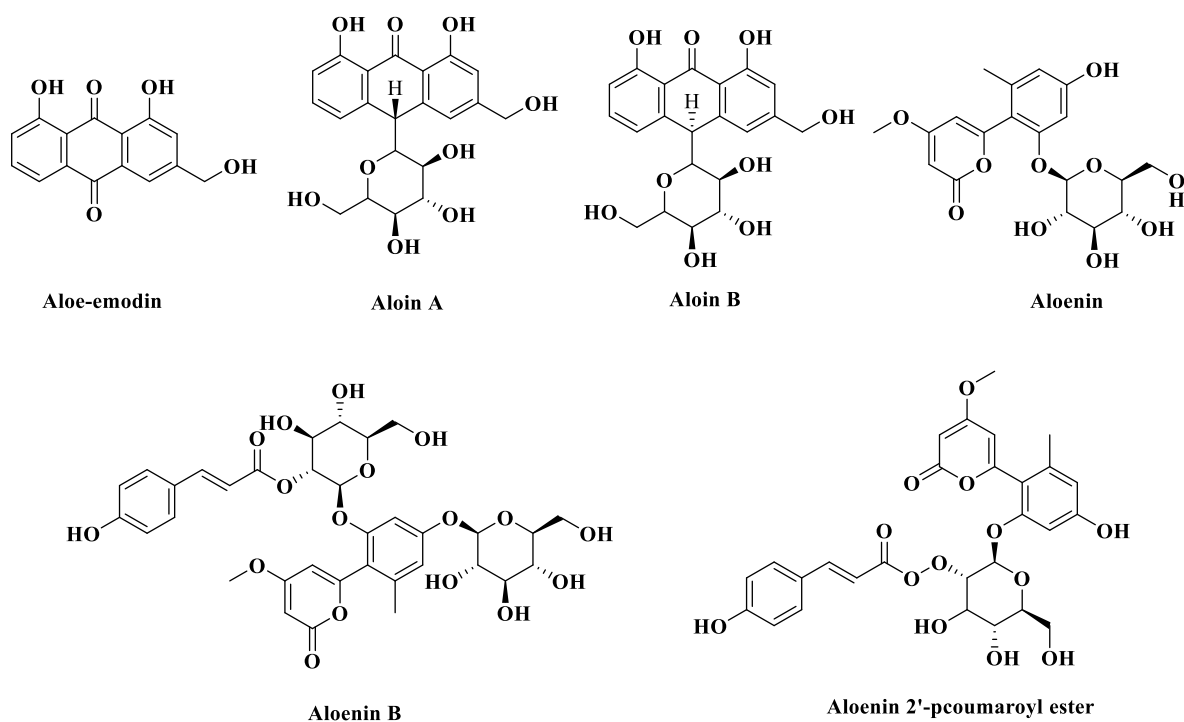
Figure 1. Major identified molecules of Aloe vera leaf extracts [11].

2. Materials and Methods

2.1. Calculation of QSAR and pIC$_{50}$.

The chemical structure and biological activity of chemical compounds are related according to the QSAR [20-22]. Quantum Stochastic Aroma Recognition (QSAR) is a quantum chemistry technique that forecasts a compound's potential for medical development. A publicly accessible website called ChemDes (http://www.scbdd.com/chemopy_desc/index/) was utilized to perform QSAR and pIC$_{50}$ [23]. Data such as Chiv5 molecular connectivity, bcutm1 mean burden descriptors, MRVSA9, MRVSA6, and PEOEVSA5 are examples of MOE type descriptors; GATSv4 indicates autocorrelation descriptors; the final two parameters, J and diameter, imply topological descriptors of drug molecules for ligands that have been reported. The parameters were first gathered from the ChemDes database to determine and calculate the QSAR and pIC$_{50}$. Next, the multiple linear regression (MLR) was developed in an Excel sheet, and the pIC$_{50}$ value was calculated using the aforementioned MLR equations.

$$pIC50 \ (Activity) = -2.768483965 + 0.133928895 \times (Chiv5) + 1.59986423 \times (bcutm1) + (-0.02309681) \times (MRVSA9) + (-0.002946101) \times MRVSA6) + (0.00671218) \times (PEOEVSA5) + (-0.15963415) \times (GATSv4) + (0.207949857) \times (J) + (0.082568569) \times (Diametert) \ [23]$$

2.2. Molecular docking.

Using the CB-Dock (Cavity-detection guided Blind Docking) protein-ligand docking approach, the selected compounds were docked with the receptor individually [24]. Compound structures were designed with the ChemSketch program and stored in the mol format. Target proteins for docking were obtained with a resolution less than 2.70 Å, R-value free of 0.274, and PDB ID (PDB ID: 1I09) from the RCSB Protein Data Bank [25]. The CB-Dock approach precisely locates the binding zone, determines the size and location of the center, adjusts the

docking region's size based on the molecules input, and then docks using AutoDock Vina version 1.1.2 [26]. Before docking, a PBD file for the receptor and a mol file for the ligands were input. Molecular docking was done at each of the several top cavities that were automatically chosen throughout this procedure and used for further investigation (cavity sorting).

3. Results

3.1. Calculation of QSAR and pIC$_{50}$.

In the field of drug discovery and design, the QSAR computer modeling technique has been utilized to forecast the biological activity of chemical compounds based on their molecular structures [21]. This is completed and mainly applied to the creation of novel medications, particularly computer-aided drug design. It entails creating mathematical models that relate structural features or physicochemical descriptions of molecules to how they function biologically [27,28].

The QSAR standard ranges are regarded as being less than 10. Theoretically, every molecule with a value less than 10 is potential [23]. The QSAR and pIC$_{50}$ overall results in our present analysis are positive (Table 1) and satisfied with standard ranges. 5.49 and 4.47 are the greatest and lowest values of pIC$_{50}$, respectively. The chemical may be therapeutically effective against the targeted ailment, according to the pIC$_{50}$ results.

Table 1. Data of QSAR calculation.

Compound Name	Chiv5	bcutm1	(MRVSA9)	(MRVSA6)	(PEOEVSA5)	GATSv4	J	Diameter	pIC$_{50}$
Aloe-emodin	1.678	4.03	11.566	58.149	12.133	1.301	1.872	9.0	4.47
Aloin A	3.286	4.045	5.783	58.149	18.199	0.95	1.734	10.0	4.99
Aloin B	3.286	4.045	5.783	58.149	18.199	0.95	1.734	10.0	4.99
Aloenin	1.967	4.0	0.0	40.249	0.0	0.916	1.768	12.0	4.98
Aloenin B	3.643	4.011	12.045	76.154	12.133	0.989	1.353	20.0	5.49
Aloenin 2'-p-coumaroyl ester	2.646	4.003	12.045	76.154	12.133	0.922	1.425	19.0	5.28

3.2. Molecular docking.

Docking analysis was conducted on all the compounds (Figure 1) using the target protein glycogen synthase kinase-3β (GSK3-β), a suitable target for identifying the agents promoting wound healing. The compounds' docking results show the best binding modes against 1I09 protein, with docking scores ranging from -7.6 to -9.5 kcal/mol, as compared to the reference molecule (sulphathiazole), which has a docking score of -6.2 kcal/mol. Regarding the target protein's active site amino acids, Figure 2 and Table 2 summarize the H-bonds and hydrophobic interactions, compound binding affinities, and 3D images of the best-fit and reference compounds. Based on the binding scores, Aloenin 2'-p-coumaroyl ester seems to fit into the 1I09 protein binding pocket more firmly and with higher binding energies than the reference molecule. Consequently, the findings of the present study demonstrate that aloenin 2'-p-coumaroyl ester is one of the most promising next-generation medications for wound healing and may be used to treat wounds as well as their accompanying symptoms. Furthermore, of all the compounds, this one has formed the greatest number of hydrogen bonds and hydrophobic interactions with the 1I09 protein.
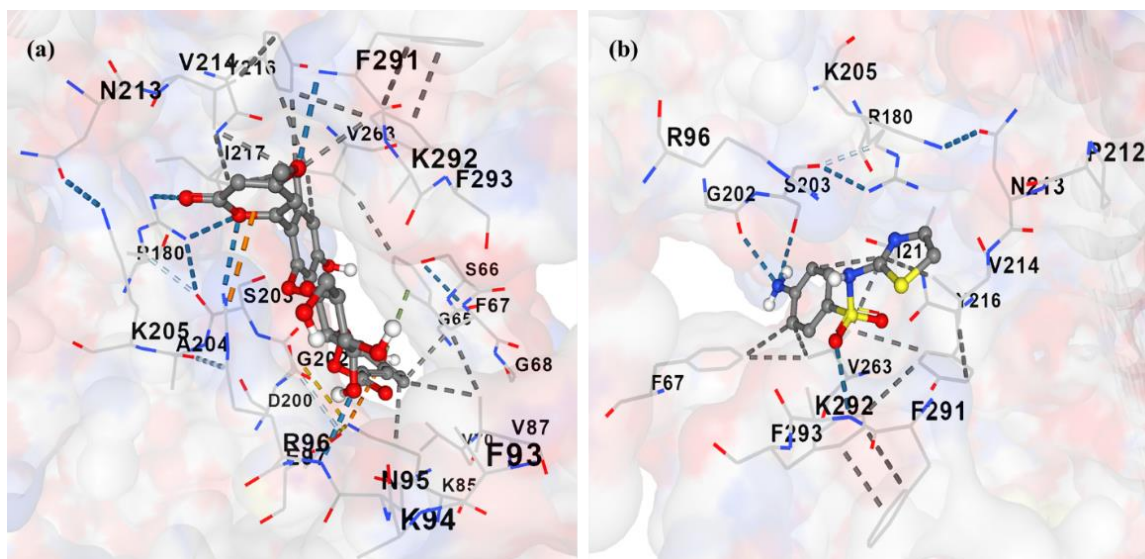
Figure 2. Molecular docking results analysis of **(a)** Aloenin 2'-p-coumaroyl ester; **(b)** reference compound (Sulphathiazole) with the target protein GSK-3β (PDB ID: 1I09).

Table 2. Molecular docking results analysis of six bioactive compounds (Figure 1) identified from Aloe vera leaves with the target protein GSK-3β (PDB ID: 1I09).

Compound Name	Cavity Size	Vina Score	Bound Amino Acids
Reference compound (Sulphathiazole)	1414	-6.2	Gly202, Ser203, Asn213 (H-B), Phe67, Val263, Ile217, Tyr216, Val214, Phe291 (C-H)
Aloe-emodin	1414	-7.8	Asn95, Glu97, Ser203 (H-B), Arg96, Ile217, Val214, Tyr216, Phe291, Phe293 (C-H)
Aloin A	1414	-8.6	Glu97, Tyr234, Ser203, Ala204, Gly202, Asn213, Lys94 (H-B), Asn213, Val214, Tyr216, Ile217, Val263, Phe67, Phe291, Phe293, Arg96 (C-H)
Aloin B	1414	-8.1	Glu97, Lys94, Gly202, Ala204, Ser203 (H-B), Val214, Try216, Ile217, Phe67, Arg96, Val187 (C-H), Lys85 (ionic)
Aloenin	1414	-7.6	Gly65, Ser66, Asn64, Asp200, Asp264, Ser261, Val69, Glu97 (H-B), Val70, Phe67, Ile217 (C-H), Lys85, Lys183 (ionic)
Aloenin B	1414	-8.4	Ser261, Asp264, Asp281, Asn186, Ser66, Asp200, Cys199, Asn95, Ile84 (H-B), Val135, Ile62, Phe67, Lys85, Val87 (C-H), Lys85, Lys183 (ionic)
Aloenin 2'-p-coumaroyl ester	1414	-9.5	Ser66, Glu67, Gly202, Ser203, Asn213 (H-B), Phe67, Asn213, Ile217, Val263, Val214, Phe291, Phe293 (C-H), Lys85 (ionic), Arg96 (pi-cation), Phe67 (pi-pi stacking)

According to the molecular docking investigation, Aloenin 2'-p-coumaroyl ester bound in the GSK3-β protein's active region with a binding energy of -9.5 kcal/mol. The residues of Ser66, Glu67, Gly202, Ser203, Asn213 (H-B), Phe67, Asn213, Ile217, Val263, Val214, Phe291, Phe293 (C-H), Lys85 (ionic), Arg96 (pi-cation), and Phe67 (pi-pi stacking) were all interacting with the aloenin 2'-p-coumaroyl ester (Figure 2a). These results, which underwent extensive analysis, suggest that Aloenin 2'-p-coumaroyl ester interacts differently with GSK3-β's binding pocket. Conversely, Figure 2b depicts the interactions that the reference molecule, sulphathiazole, displayed with the residues of Gly202, Ser203, Asn213 (H-B), Phe67, Val263, Ile217, Tyr216, Val214, and Phe291 (C-H).

4. Discussion

Through a variety of strategies, naturally produced bioactive compounds significantly improve wound healing and tissue regeneration [29]. Aloe vera leaves have been utilized extensively in both pharmaceutical and cosmetic applications. Moreover, this medicinal herb

has historically treated skin burns, wounds, and inflammation. Aloe vera has further proven to provide a number of health benefits, including antihyperlipidemic, antioxidant, anticancer, and antidiabetic properties [30]. This work investigated the main compounds from Aloe vera for their ability to induce the Wnt signaling pathway and promote wound healing through GSK3-β inactivation. Our findings showed that Aloenin 2'-p-coumaroyl ester interacted with the active site of GSK-3β protein with the best affinity.

People can use many secondary metabolites found in plants to cure a variety of illnesses. Numerous therapeutically effective medications crucial to the treatment of illnesses have been found due to the existence of phytochemicals extracted from natural sources like plant extracts and microbial fermentation. Plant-based natural compounds are useful in enhancing the effects of medications on microbial interactions. Because of their antibacterial, antipyretic, hepatoprotective, anticancer, anticoagulant, anti-inflammatory, antiparasitic, wound-healing, and immunosuppressive properties, plants are useful in treating several disorders [31]. *Aloe vera*, *Sophora flavescens*, *Punica granatum* L., *Mimosa pudica* L., and *Hibiscus rosa sinensis* L. are among the plants and plant products that have been utilized in traditional medicine to treat and prevent illnesses, particularly wounds [32]. The active site of GSK3-β protein had a binding affinity of -13.457 kcal/mol for the isolated Ursolic acid from *Clematis gouriana* [31]. Additionally, Luteol, the main component of *Tamarindus indica* L., has the highest advantageous binding affinity for GSK3-β, with a binding energy of -12.5 kcal/mol [32]. Aloenin 2'-p-coumaroyl ester had the greatest binding affinity in this investigation, with a value of -9.5 kcal/mol in the active site of GSK3-β protein.

The fundamental foundations of wound healing and regeneration are cell signaling pathways, such as the Wnt/β-catenin and FGF/TGF-β pathways. A disruption in their release may impact the function of fibroblast cells and the healing of wounds. The Wnt/β-catenin pathway is important for wound healing because it promotes cell proliferation [33]. The GSK3-β enzyme, which phosphorylates and degrades the β-catenin protein, is this route's most significant signaling intermediary. β-catenin is activated and translocates into the nucleus in response to inhibition of GSK3-β, which controls the expression of certain genes. Previous research employing several animal models indicates that small compounds, including inhibitors of glycogen synthase kinase 3-β (GSK3-β), are helpful tools for accelerating the healing process of wounds [29].

In several contexts, it has been demonstrated that the phosphoinositide 3-kinase (PI3K)/Akt pathway is essential for controlling mitogenic signaling, apoptosis, cell division, and survival [34]. By phosphorylating phosphatidylinositol, phosphatidylinositol-4-phosphate, and phosphatidylinositol-4,5-bisphosphate, PI3K catalyzes the synthesis of phosphatidylinositol-3,4,5-triphosphate. This phosphorylation process is initiated by growth factors and hormones [35]. Akt, also known as protein kinase B or Rac, is involved in a PI3K-dependent wortmanninsensitive pathway [36]. 3-A key player in the PI3K/Akt pathway, phosphoinositide-dependent protein kinase-1 (PDK1), is responsible for activating Akt. Through its capacity to phosphorylate and inactivate a number of substrates, including Bad, forkhead transcription factors (AFX, FKHR, and FKHRL1), caspase-9, and glycogen synthase kinase-3b (GSK3-b), Akt supports cell survival by preventing apoptosis. One important negative regulator of the PI3K/Akt signaling pathway is phosphatase and tensin homolog deleted on chromosome 10 (PTEN) [35].

Naturally occurring compounds with therapeutic qualities can aid in the healing process of wounds. Much research has been done on the ability of natural compounds with anti-

inflammatory, antioxidant, antibacterial, and pro-collagen synthesis capabilities to heal wounds. The bioactive phytochemical components of the many chemical families, including tannins, terpenoids, alkaloids, essential oils, flavonoids, saponins, and phenolic compounds, may have contributed to their therapeutic qualities [37]. Every bioactive substance may have a unique role in the qualities of wound healing. For example, tannins and flavonoids have antiseptic and antibacterial properties, while saponins can increase pro-collagen production. These phytochemicals have the ability to alter one or more stages of the healing process for wounds [38]. Moreover, the epidermal layers of the skin readily absorb them. Owing to these characteristics, natural products and the phytochemicals they play significant roles in the healing of wounds and are utilized in the creation of novel synthetic compounds intended for this usage [37].

The molecular docking tools and the quantitative structure-activity relationship model (QSAR) are two of the most effective computational approaches for drug discovery research. QSAR aims to establish a rational, mathematical link between biological activity and chemical structural attributes. Descriptors, or numerical numbers that characterize a compound's structure, are chemical attributes associated with its structures. Correct knowledge about the structural patterns that have an appropriate link with the intended activity of a drug-like chemical is provided by a reliable and valid QSAR model. The described QSAR models are suitable for the common applications of accurate QSAR models, which are centered on the estimation of biological activities of novel compounds with structures similar to the major structure in the data set, and they have a desired level of accuracy [39]. The MLR QSAR model's component molecular descriptors have revealed prominent and obscure details on the structural characteristics of a wide range of compounds examined in the current QSAR research for their potential to promote wound healing. It is critical to realize that, given such a heterogeneous collection of molecules, no one molecular descriptor can account for all of the observed dispersion. In other words, the effectiveness of the created QSAR model depends on the concurrent application of the component molecular descriptors.

Using the CB-Dock program, we employed a blind docking technique in this investigation. CB-Dock is a protein-ligand blind docking technique that uses AutoDock Vina to execute molecular docking after automatically determining the binding sites, their size and center, and tailoring the docking box size to the query ligands. Benchmarks on a large scale demonstrate that cavity-targeted docking can improve blind docking's hit percentage and accuracy. As a result, by predicting the binding sites of target proteins using the curvature-based cavity detection technique (CurPocket) and the binding poses of query ligands using AutoDock Vina, CB-Dock may speed up the docking process and increase accuracy. For this reason, grid coordinates also varied for every ligand [40].

One of the most valuable applications of QSAR research, which has attracted a lot of interest lately, is the generation of novel, potent drug suggestions using QSAR models. The developed association between the biological activities and the interpretable but restricted descriptors serves as the foundation for recommending novel compounds. Thus, when the suggested QSAR models are sparse and have high accuracy, utilizing them will be successful. Because of this idea, just a select few of the most significant descriptors should be used to construct the QSAR model. We selected the chemicals for docking investigation with the GSK3-β protein from the QSAR study.

The molecular docking research of Aloe vera's main constituents using GSK3-β was accomplished successfully. A strong binding affinity between the ligands and the protein was

demonstrated by the lowest binding energy, which was determined to be between -9.5 and -6.2 kcal/mol. Aloenin 2'-p-coumaroyl ester was found to have the lowest binding energy of all the ligands, at -9.5 kcal/mol. This investigation verified that Aloenin 2'-p-coumaroyl ester interacts to GSK3-β via hydrophobic contacts at positions Phe67, Asn213, Ile217, Val263, Val214, Phe291 and Phe293 and by hydrogen bonds at places Ser66, Glu67, Gly202, Ser203, and Asn213 (Figure 2a). These results show that GSK3-β, an essential component of the Wnt pathway that is essential for wound healing, may be inactivated by aloenin 2'-p-coumaroyl ester. Substrate recognition requires contact with GSK3-β residues, Phe67, Gln89, and Asn95, which offer a common foundation for substrate binding and selectivity yet allow for substrate variety [41]. Prior phosphorylation is often needed in GSK3-β substrates. In the event of diabetes mellitus, the Aloenin 2'-p-coumaroyl ester will be the preferred option for the quicker healing of chronic wounds. Nevertheless, more research on animals is needed to validate the efficacy of aloenin 2'-p-coumaroyl ester.

To provide a fair evaluation, it is important to highlight the numerous drawbacks associated with the use of the most recent in silico methods. The assurance and openness of the high-quality experimental data used to construct the training data set and the understanding of precisely what is being modeled for the QSAR model's user base are the limiting criteria for predictive QSAR modeling. The use of a false data point that resulted in an incorrect forecast is referred to as amplification. It may also refer to situations when several computing platforms use the QSAR training data sets to create a model or where inaccurate data is repeatedly used to optimize or update a new model. Thus, great care and attention to detail must be taken to guarantee that the highest caliber and most readily available experimental data are incorporated into the model. Additional restrictions on the QSARs that are now accessible concern the absence of models for complex mixes (like botanical extracts), large molecular weight compounds (like polymers), and organometallics. It is also important to note that QSAR models for rodent carcinogenicity have essential limitations [42]. Others who are aware of the limits of the technology suggest integrating computational tools with the experimental setting in a sensible way by fusing in-silico predictions with biological data obtained in real-time (Jolivette and Ekins). The efficacy of this notion is demonstrated in some cases, such as the publication of liquid chromatography/mass spectrometry spectra paired with in silico prediction of drug metabolite structures [43]. Finding the proper chemical descriptors to help create a model and enhance prediction performance for the modeled endpoint is a significant drawback of in silico technologies. Descriptors can be produced automatically using techniques like genetic algorithms or tests chosen based on performance [44].

The drug development process aims to find bioactive molecules to help cure ailments. The in-silico approach is one way to increase the efficacy of innovative drug development. It shortens the time it takes to create new drugs and lowers overall research costs by using molecular modeling to realistically screen a large number of compounds for drug-likeness features and their interaction with pharmacological targets. A developing computational technique for identifying a bioactive Compound's most likely targets and, thus, foreseeing adverse responses, side effects, and medication repurposing is a compound in silico activity profiling. It may be used in various contexts, such as multitarget methods, medication repositioning, and natural product profiling [45].

Aloenin 2'-p-coumaroyl ester (([[(2S,3R,4S,5S,6R)-4,5-dihydroxy-2-[4-methoxy-6-oxopyran-2-yl]-3-methylphenoxy-5-hydroxy-2-]3-yl -6-(hydroxymethyl)oxan] Aloe vera's principal phytocompound, (E)-3-(4-hydroxyphenyl)prop-2-eneperoxoate, has the molecular

formula $C_{28}H_{28}O_{13}$ (Figure 1). It was discovered to contain a higher percentage of derivatives of phenyl pyrone, ranging in concentration from 16.204 to 38.762 mg/g. It is likewise a phenyl pyrone, and it was interesting that other phenyl pyrones could be detected using similar fragmentation behavior [46]. OATP2B and BSEP may be inhibited by aloenin 2'-p-coumaroyl ester [11].

In conclusion, it was demonstrated that aloenin 2'-p-coumaroyl ester had an excellent pIC_{50} value of 5.28, which was less than 10. With a binding energy of -9.5 kcal/mol, the docking result indicates that aloenin 2'-p-coumaroyl ester has a considerable affinity for the active area of the GSK3-β protein. Aloenin 2'-p-coumaroyl ester can potentially be a wound-healing agent by inhibiting the activity of the GSK3-β protein, as indicated by the findings and discussion.

5. Conclusions

To properly cure wounds, novel chemical development with potential biological activity and minimal to nonexistent side effects is desperately needed. The GSK3-β protein's active site was successfully docked with aloenin 2'-p-coumaroyl ester. Using the CB-Dock program, the docking score of the aloenin 2'-p-coumaroyl ester was ascertained. The interactions of GSK3-β include hydrogen bonds, hydrophobic contacts, π-cation interactions, π-π stacking, and ionic interactions. Docking scores, however, support the hypothesis that considerable wound healing characteristics may result from upregulating GSK3-β. According to the study's findings, these might potentially form the basis for developing new wound-healing agents that can be effectively utilized in the future to treat wound healing. There is a need for additional molecular biology study on cell culture and/or animal studies in order to address the potential biological activity of Aloenin 2'-p-coumaroyl ester with GSK3-β.

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Acknowledgments

Conflicts of Interest

No.

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