GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 2 (359) Февраль 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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Содержание:

GEORGIAN MEDICAL NEWS
No 2 (359) 2025

IN SILICO DOCKING OF SILYMARIN ACTIVE CONSTITUENTS WITH INSULIN RECEPTORS: A STEP TOWARD DIABETES THERAPEUTICS

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Abstract.

Given its impact on glucose metabolism, the insulin receptor (IR) is considered one of the key focus areas for medical intervention in people suffering from diseases, such as diabetes mellitus. Silymarin, a natural flavonoid complex obtained from Silybum marianum (milk thistle), has been used and is known for its antioxidant and anti-inflammatory mechanisms; however, the possible effects of these compounds on the insulin receptor are yet to be fully explored. In this study, molecular docking was carried out to ascertain the binding and interaction of the active components of silymarin, such as silybin, silychristin, and silydianin, with the insulin receptor. The results from the docking simulations showed that silybin, the most important silymarin's active component, possessed relatively higher binding energies and interacted with the important key residues in the extracellular domain of the insulin receptor, suggesting possible effects on receptor activation and downstream signalling pathways that are involved in insulin's action. Moreover, the active sites on the insulin molecule possess equivalent potentials to those of silymarin, suggesting their capacity to attach to the insulin receptor. This molecular basis has led to clinical studies looking for a mechanism for which silymarin functions to alter insulin signaling, which can be targeted for the treatment of patients battling insulin resistance and diabetes. Such interactions and the possible use of such compounds in therapies can be further proved by cytometric and molecular studies depicting the usage of molecular dynamics simulations.

Key words. Milk thistle, silymarin, insulin receptor, molecular docking, CHD metabolism.

Introduction.

Silymarin has been understandably studied in depth and is considered to be an important substance of assorted natural active ingredients with protective effects for the liver [1]. This very natural product is mainly composed of four different structurally related flavonolignans and an accompanying flavonoid taxifolin [2]. Silymarin has gone through extensive and detailed preliminary studies and has been proposed to be of health benefit to the liver in numerous studies, supporting the findings in humans [3]. For example, patients presenting with different liver diseases can certainly benefit from using silymarin. Hence, from a theoretical point of view, we contemplated whether silymarin can be utilized in the health of different tissues or organs of the body [4]. Of course, the answer could be affirmative. One critical issue pertains to carbohydrate metabolism, which occupies central significance in bodily operations, represents one of the important substances used in response or resistance, and indicates people's health conditions [5,6].

So far, the researchers have provided a full and comprehensive understanding of the complex processes of carbohydrate metabolism. Unsurprisingly, several issues remain to be clarified, such as the precise mechanism governing carbohydrate metabolism [7]. At the same time, some limitations and inadequacies may occur in the assessment parameters of carbohydrate metabolism. We therefore attempted to conduct a theoretical, albeit speculative, study to examine the dilemma surrounding sugar consumption and identify some drawbacks in the flesh [8]. Subsequent discussions on the role of silymarin compounds are additionally featured in the present essay, to launch investigations to assess the appropriateness thereof.

Carbohydrate metabolism plays a crucial role in boosting the energy reserves necessary to maintain normal physiology. Any pathology related to carbohydrate metabolism directly or indirectly affects body health. Several medications are used to maintain glucose and lipid metabolism [9]. Conventional as well as alternative systems of medicine have been explored to modulate metabolic pathways. Silymarin is a standardized extract of milk thistle seeds. The silymarin extraction process is divided into two steps. The plant's fruits undergo a six-hour defatting process, followed by a five-hour extraction of silymarin using solvent methanol. Pressurized liquid extraction is an alternative approach to harvesting silymarin, which involves using extractants at high pressure and temperatures higher than their boiling point [10]. Silmarin contains a mixture of at least seven flavolignans like silybin, isosilybin, silychristin, silydianin, taxifolin, dihydrosilydianin, silybinin, and five flavonoids like silychristin, silydianin, silydinosin, silyhermin, and kaempferol. It has been used as a potent liver-tempering agent. This drug has a promising role in the treatment of enzyme improvers to modulate different metabolic pathways [11]. Studies on several in vitro and in vivo systems suggest an interesting relationship between silymarin bioavailability and action; they discuss the hypothesis that complex homeostatic mechanisms tend to oppose the accumulation of silybinin in the body since its clinical usage seems to promise several advantages in treating metabolic disorders [12].

The proliferating rate of hepatocytes can be manipulated by the usage of bioactive compounds. Silymarin is one of these bioactive compounds, clinically reported to have multifarious uses; specifically, it has beneficial roles to play in the modulation of liver-specific enzymes and gene expression to regulate liver glucose and lipid homeostasis. Carbohydrate metabolism is indeed a very intricate, complex interaction of multifactorial regulation [13,14]. Metabolic dysfunctions are difficult to deal with, particularly linked to diabetes, as hepatic glucose production and ROS levels that down-regulate glucose uptake and glycogen synthesis are modulated in part by silymarin compounds in in vitro experimental conditions [15].

The research aim of the proposed work is to perform an in-depth study of the role of silymarin compounds, in particular silibinin and silybin, in the regulation of various processes of carbohydrate metabolism [16]. The main research question is to investigate the effect of silymarin on carbohydrate metabolism: is it possible to change the intensity of individual pathways of carbohydrate metabolism without changes in body weight, basal levels of insulin, and glycemia? How are the glucose homeostasis indices changing with increased production of glucose by the liver or its consumption by the muscle in parallel with the intake of silymarin? This study is of basic and practical importance since it may be beneficial for people who need to regulate the rate of glucose uptake by muscle or the rate of endogenous glucose synthesis, as well as for the dietary supplement industry [17,18]. People who exercise, have prediabetes, type 2 diabetes, obesity, or polycystic ovary syndrome often have high insulin levels, and silymarin can increase insulin sensitivity in this group of people and contribute to their health. The main objectives are to perform a literature review on the role of mainly silibinin and silybin in the regulation of selected steps of carbohydrate metabolism and glucose homeostasis, in particular in the group of people with type 2 diabetes; perform in vitro laboratory studies on the effect of silymarin, and above all silibinin and silybin, on the carbohydrate metabolism pathway with particular attention to the effect on the intensity of AMPK and ACC activity, the effect on GLUT4 and PPARγ expression, and the effect on the use of glucose in the muscle and liver. It is also planned to analyze the changes in the activity of liver and muscle transaminases, biomarkers of liver and muscle injury, and ALT and AST as indicators of liver injury. The results of the research on the use of silymarin compounds in carbohydrate metabolism in diabetes will have health implications and contribute to the knowledge of the role of silymarin in health and nutrition [19,20].

Silymarin and its constituents, silybin and silybin, exhibit diverse biological activity, including hepatoprotective, anticancer, antiviral, antiangiogenic, anti-inflammatory, antioxidative, and immunomodulatory effects [21]. The antioxidant property of silymarin can slow down the ageing process and can prevent or treat some diseases. Although largely known for its hepatoprotective action, silymarin also interferes with glucose and lipid metabolism [22].

Expanding further the interests of the research community, this article discusses the potential role of silymarin with its bioactive constituents and also provides detailed insights into their mechanism of action. These insights may pave the way for intervention in the carbohydrate metabolism system. Thus, further identification and clarification of the bioactivity of silymarin compounds are indispensable. These could be applied to clinical conditions regarding metabolic health, especially for diabetes mellitus and obesity, including mechanisms.

The interactions between silymarin compounds and carbohydrate metabolism are the focal point of our theoretical research. These interactions influence carbohydrate metabolism and may impact many metabolic pathways [23]. Several studies conducted at the experimental level have attempted to explain these interactions; many of them explain how silymarin enhances insulin functioning and how silymarin compounds reduce glucose processing and homeostasis. Additionally, recent studies show that silymarin compounds can be depicted in the form of a theoretical model. Thus, in this study, we present the combined information and explain these data in terms of practical applications in health and nutrition [24].

Regarding the percentage of active components in silymarin: Silymarin is primarily composed of flavonolignans, with silybin (both silybin A and B) being the most abundant and active component, typically constituting about 50-70% of the extract. The remaining components, such as silychristin and silydianin, account for the rest of the composition, with their contributions being relatively smaller [11]. This study aimed to an in-silico investigation of the molecular docking interactions between silymarin and insulin receptors.

Materials and Methods.

The docking study was the interaction between silymarin and insulin receptors using the program (MCULE). Mcule.com is an online drug discovery platform. It offers a unique solution for pharma and biotech companies by providing the highest quality purchasable compound database and molecular modelling tools. The Chem-Bio Office 3D (version 17.1) was used to create the pharmaceutical molecules. Using an Intel Core (i5-4810) laptop computer with 8 GB of RAM and Microsoft Windows 11 Pro as the operating system, docking for ligands and receptors is computed [25].

Results and Discussion.

The docking investigation was used to predict the interaction between different compounds (e.g. silymarin) and insulin receptors. The activity of these compounds in diabetes mellitus type 2 was taken when they were chosen [26,27]. The insulin receptor is a glycoprotein with a molecular weight of about 300 kDa. Figure 1 shows the complete formula of insulin receptors [28].

Docking with medicines, the binding score energy of the (6xbg) protein was calculated. This is shown in Table 1. The compounds predicted are listed in Figures 2-8. The docking score measures the strength of the interaction of two molecules based on shape complementarity, electrostatics, van der Waals forces, hydrophobic interactions, and hydrogen bonding [29]. A lower score (more negative) indicates a more stable and beneficial binding relationship. The algorithm evaluation examines the complex comprising the ligand (a tiny chemical, e.g., a medicine) that binds to the receptor (a protein). The greater the negativity of the energy, the stronger and more stable the binding interactions [30,31].

Table 1. *Best score of insulin receptor matching with silymarin compounds.*

	compound	Insulin receptor best score (kcal/mol)
1-	Taxifolin	-7.3
2-	Silychristin	-8.0
3-	Silydianin	-8.5
4-	Silybin A	-8.1
5-	Silybin B	-9.1
6-	Isosilybin A	-7.2
7-	Isosilybin B	-8.1

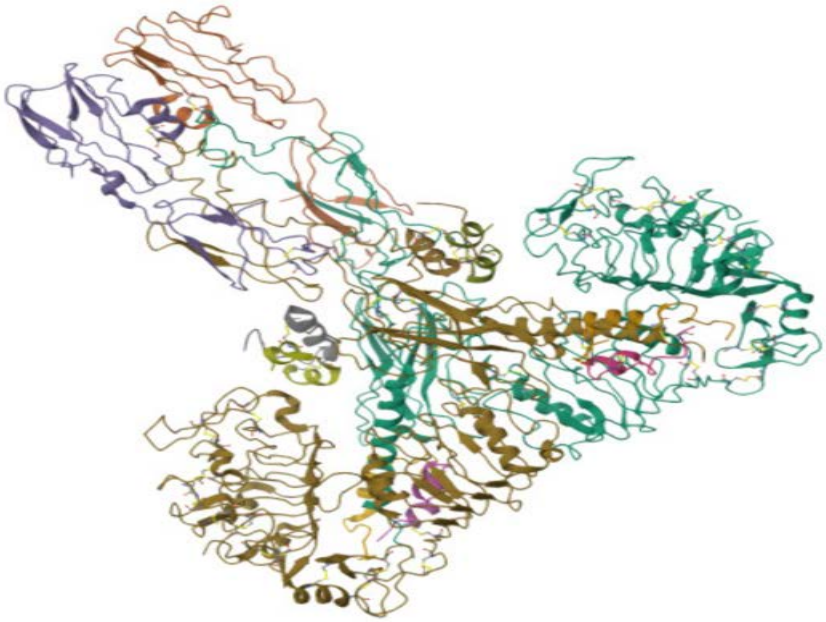

Figure 1. *Structure of insulin receptor.*

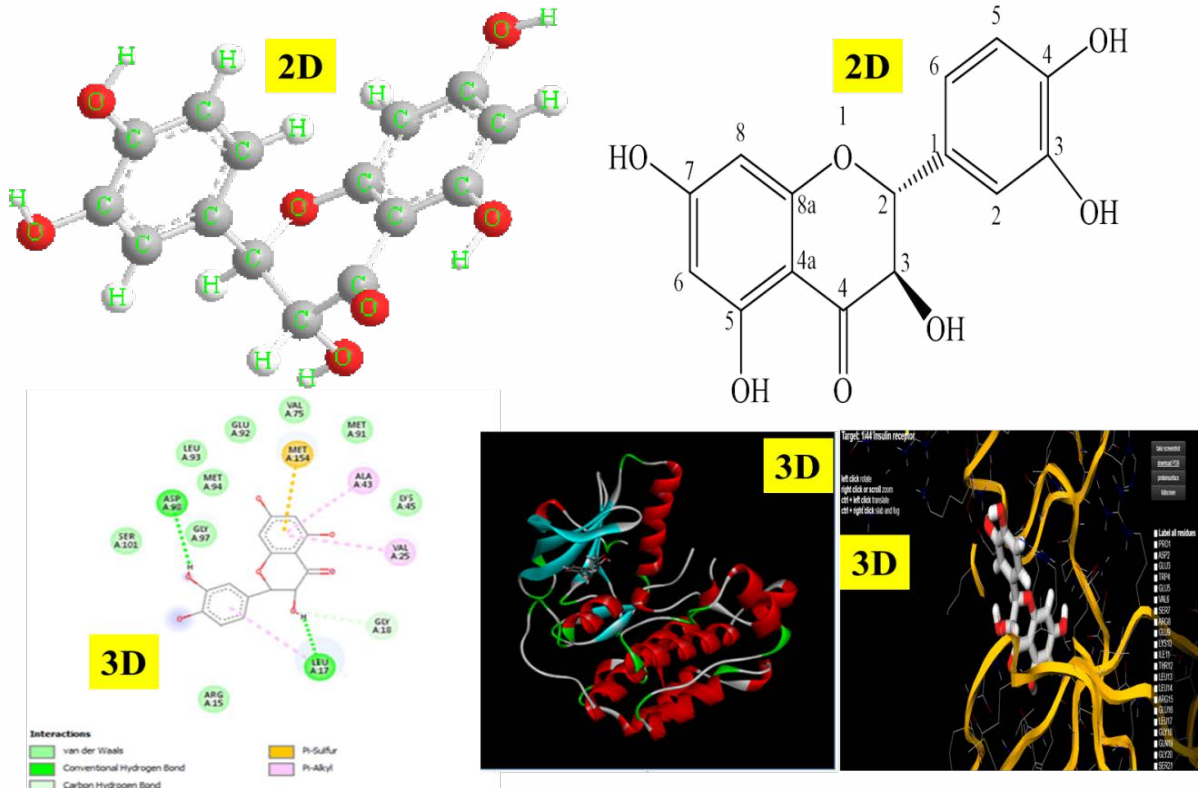

Figure 2. *The 2D and 3D structure of taxifolin [(2R,3R)-2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychroman-4-one].*

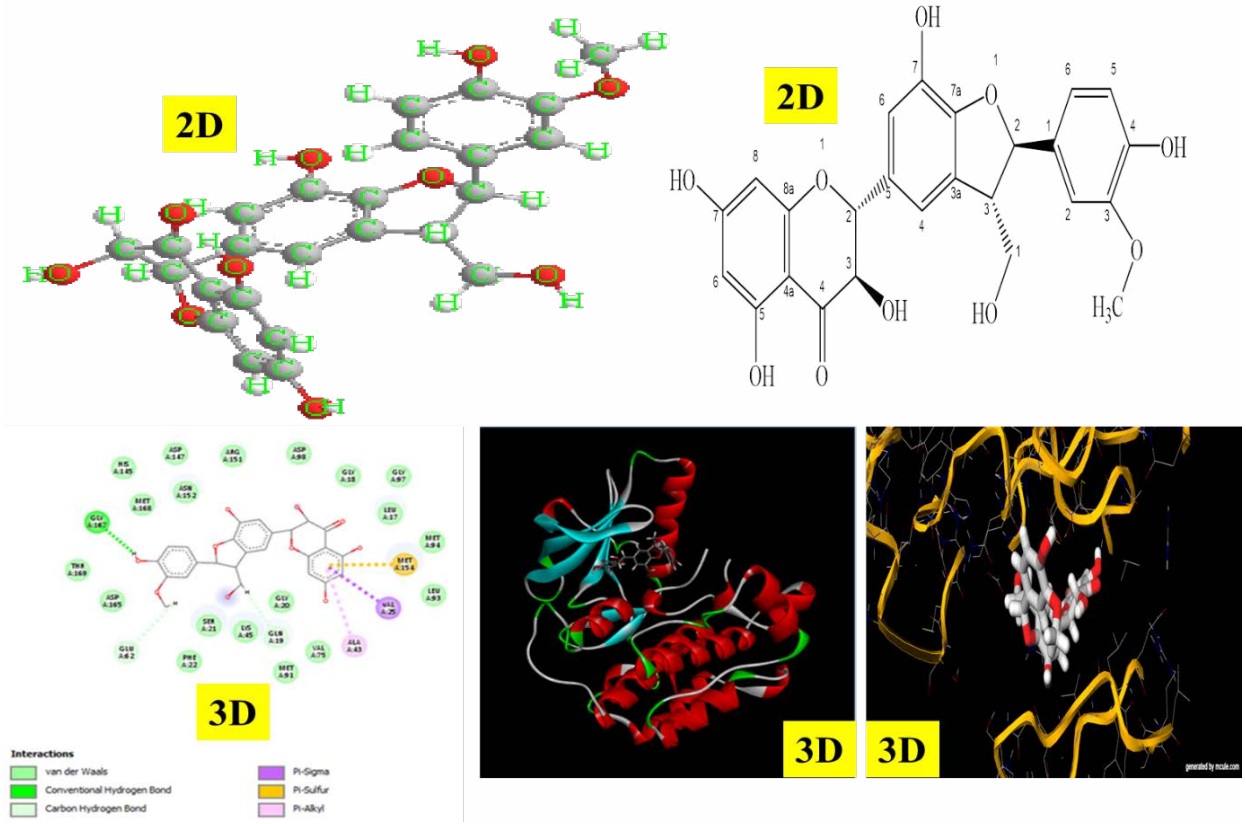

Figure 3. *The 2D and 3D structure of silychristin [(2R,3R)-3,5,7-trihydroxy-2-((2R,3S)-7-hydroxy-2-(4-hydroxy-3-methoxyphenyl)-3-(hydroxymethyl)-2,3-dihydrobenzofuran-5-yl)chroman-4-one].*

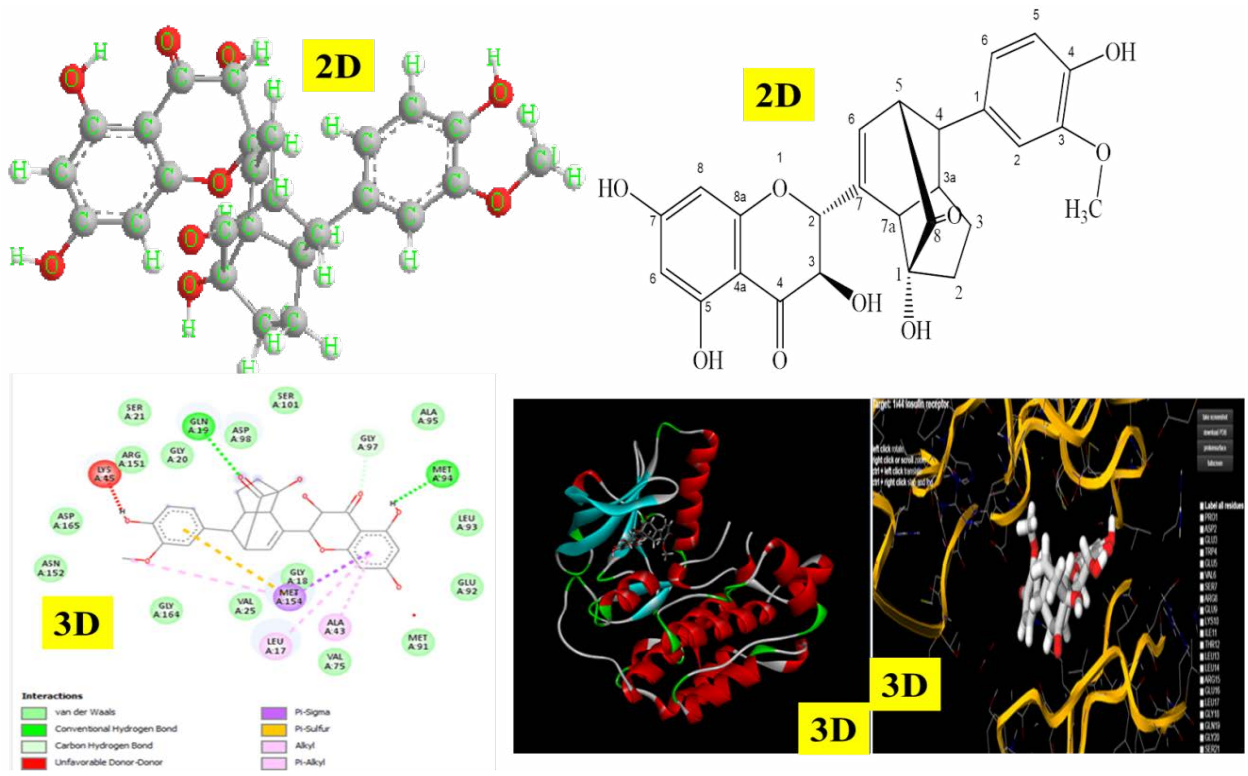

Figure 4. *The 2D and 3D structure of silydianin [(2R,3R)-3,5,7-trihydroxy-2-((1S,5R)-1-hydroxy-4-(4-hydroxy-3-methoxyphenyl)-8-oxo-2,3,3a,4,5,7a-hexahydro-1H-1,5-methanoinden-7-yl)chroman-4-one].*

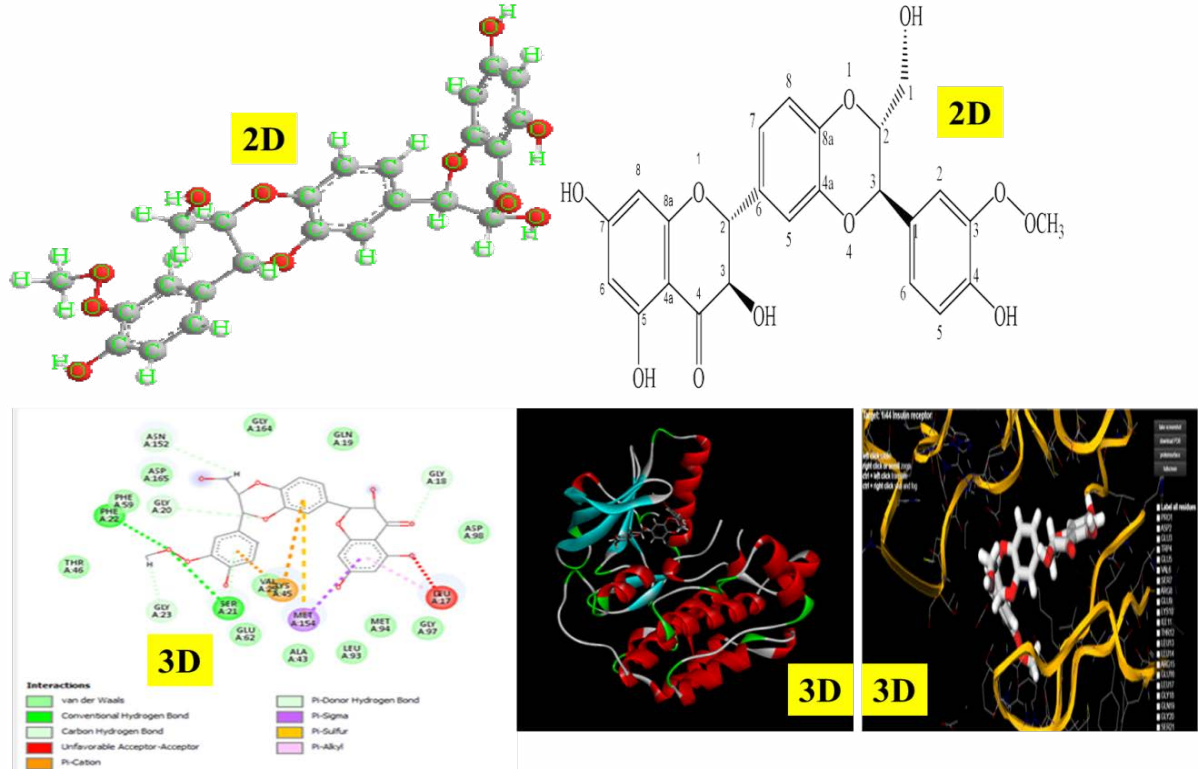

Figure 5. *The 2D and 3D structure of silybin A [(2R,3R)-3,5,7-trihydroxy-2-((2R,3R)-3-(4-hydroxy-3-(methylpeooxy)phenyl)-2-(hydroxymethyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)chroman-4-one].*

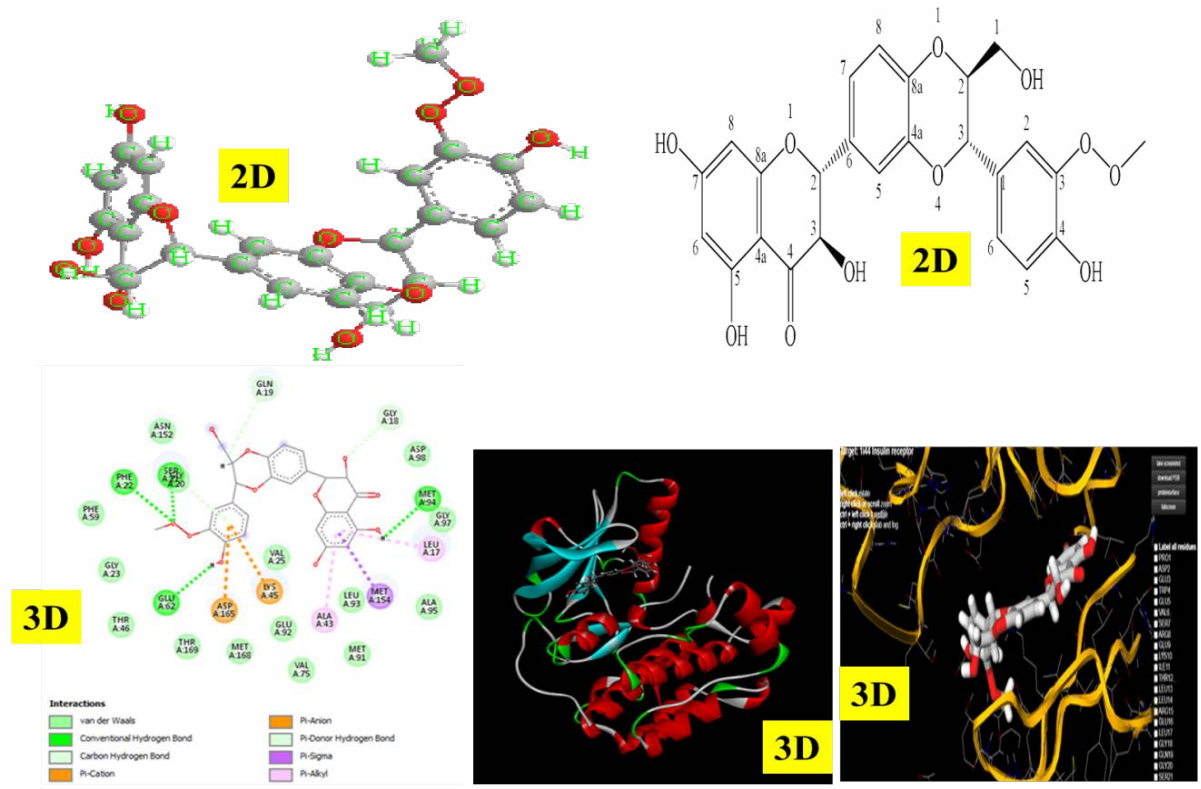

Figure 6. *The 2D and 3D structure of silybin B [(2R,3R)-3,5,7-trihydroxy-2-((2S,3S)-3-(4-hydroxy-3-(methylperoxy)phenyl)-2-(hydroxymethyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)chroman-4-one].*

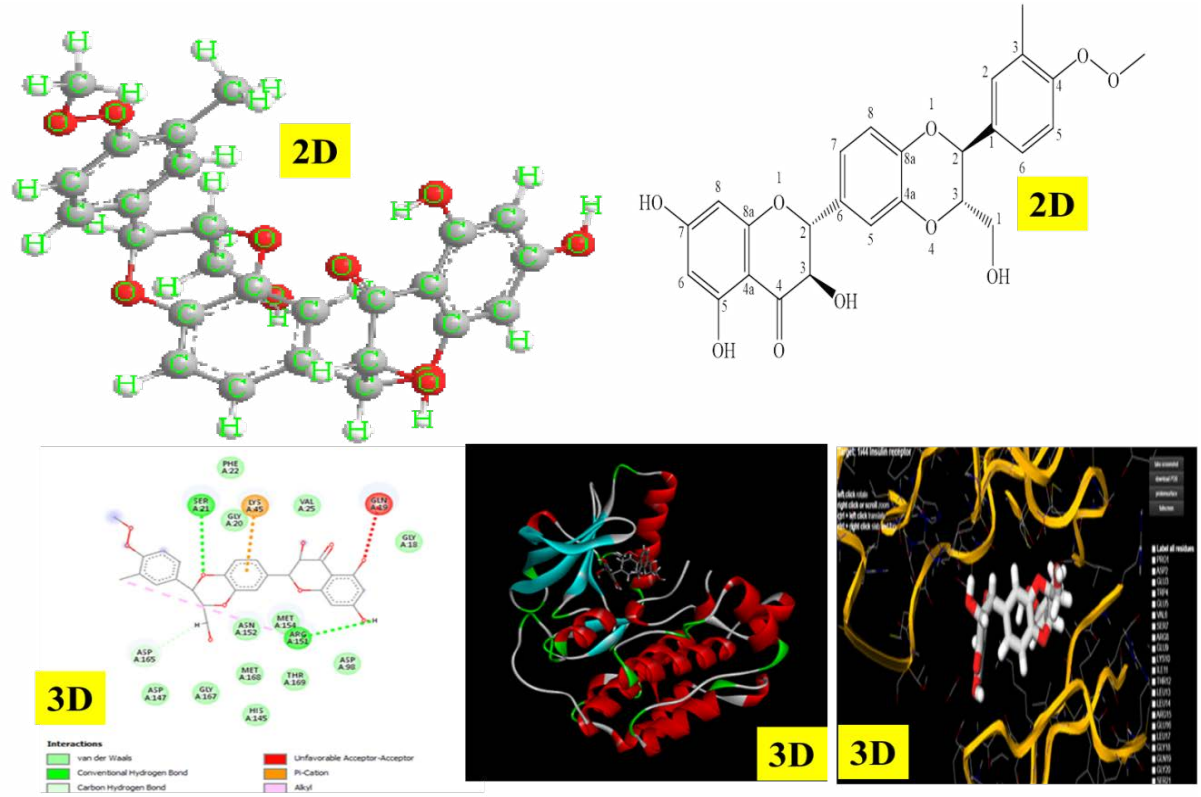

Figure 7. *The 2D and 3D structure isosilybin A (2R,3R)-3,5,7-trihydroxy-2-((2S,3S)-3-(hydroxymethyl)-2-(3-methyl-4-(methylperoxy)phenyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)chroman-4-one.*

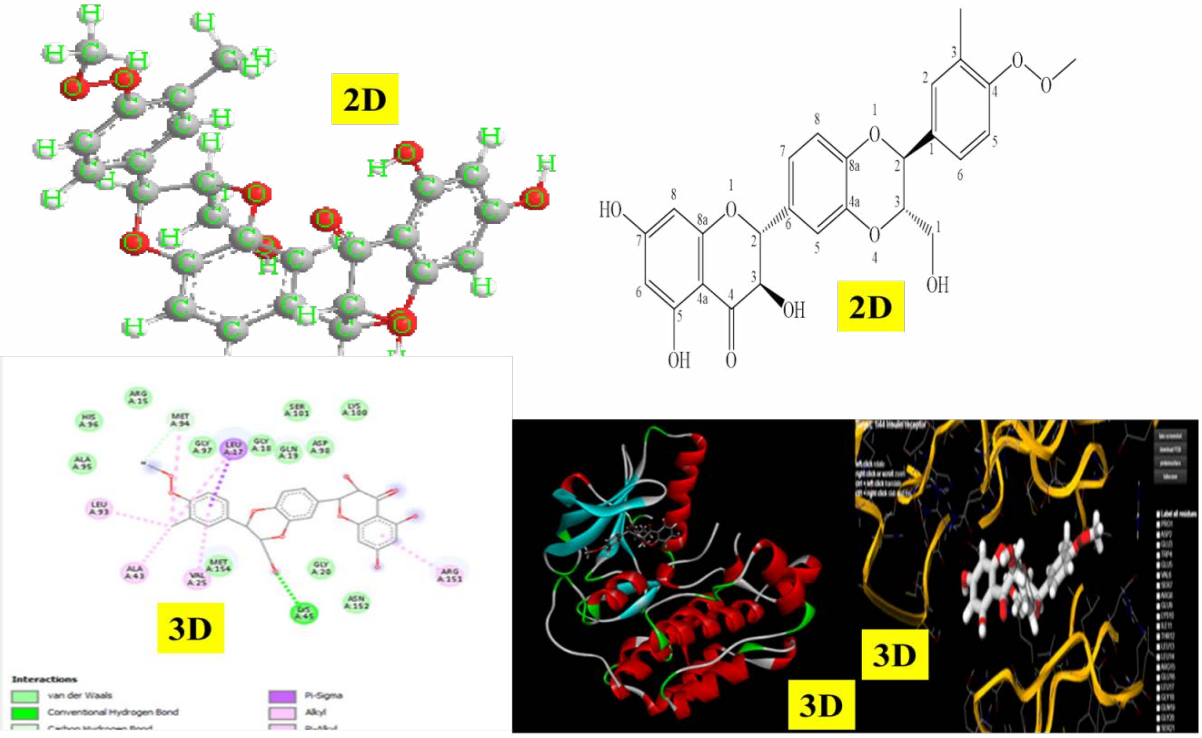

Figure 8. *The 2D and 3D structure isosilybin A [(2R,3R)-3,5,7-trihydroxy-2-((2R,3R)-3-(hydroxymethyl)-2-(3-methyl-4-(methylperoxy)phenyl)-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)chroman-4-one].*

A score range of -6 to -10 kcal/mol indicates a moderate to high interaction or binding. A score value below -10 kcal/mol is indicative of exceptional binding. If the docking score is elevated (e.g., less negative or, more significantly, positive), it indicates that the ligand may not bind well to the receptor 2. Regarding the strongest binding, the results indicate that Silybin B possesses the most negative docking score (-9.1 kcal/mol), suggesting a strong likelihood of superior binding affinity for the insulin receptor among all examined compounds. The Silybin B 3D interaction model shows that Silybin B forms several hydrogen bonds with glutamine or serine residues and has strong hydrophobic interactions with the receptor; this matches its strong docking score and renders it a promising option for further evaluation. Moderately Strong Binding: Silydianin (-8.5 kcal/mol) and Silybin A (-8.1 kcal/mol) exhibit considerable binding affinities, suggesting their potential significance in modulating insulin receptor activation. Silychristin (-8.0 kcal/mol) and Isosilybin B (-8.1 kcal/mol) demonstrate comparable binding affinity to Silybin A, indicating moderate to high receptor engagement.

Weaker Binding: Taxifolin (-7.3 kcal/mol) and Isosilybin A (-7.2 kcal/mol) interact with less relevant or weaker residues; thus, they have the lowest binding affinities among the evaluated substances. The 3D model shows that Taxifolin doesn't form many stable interactions, or its hydrophobic region doesn't interact well with the receptor; this matches its weaker docking score. Although these values still suggest the potential for interaction with the insulin receptor, the binding affinity is relatively lower compared to the other compounds. They may still exert an influence, but additional testing is required to validate their biological significance. General Estimates of Insulin's Docking Score: In some docking investigations, the docking score of insulin (depending on receptor structure and software) can be found to be around −7.0 kcal/mol–9.0 kcal/mol. Receptor and ligand structures, docking programs and parameters, conformational changes of the insulin receptors, and binding interactions with key residues, including tyrosine, glutamine, and serine, have been some of the noted factors influencing the docking score of the insulin [32,33].

Conclusion.

This study aimed to observe and study natural compounds obtained from several sources to determine their potential effectiveness in interacting with the amino acids present in the insulin receptors. We intended to determine the affinity and specificity of silymarin compounds by determining their molecular interactions with insulin receptors that may help in the formulation of new treatment methods for insulin-related diseases such as diabetes. In addition, the binding potential of these compounds was also determined to understand their optimal localization within the molecules and the role that their structure and orientation play in their effectiveness. The results indicate that these compounds, especially Silybin B, possess a substantial affinity for the amino acid residues of insulin receptors, which could suggest they may function as insulin mimetics or insulin sensitizers. Silymarin's ability to mimic insulin binding and activate the insulin receptor suggests its potential as a complementary therapy for diabetes. Besides improving insulin sensitivity, silymarin's antioxidant and anti-inflammatory effects could help mitigate diabetes-related complications. To harness silymarin's potential, strategies like nano-formulation or liposomal delivery could improve its bioavailability. Combining silymarin with insulin therapy or oral antidiabetic drugs may enhance overall treatment efficacy. Additionally, isolating and optimizing active constituents like silybin could improve its potency as an insulin receptor agonist. Further, such research will extend these interactions and focus on the clinical significance of these interactions in practice through in vitro and in vivo studies.

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