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In Silico Molecular Docking Studies and Pharmacokinetic Property Analysis of Phytocompounds from *Camellia sinensis* Targeting MCM2 Protein as Anti-Cancer Agent

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Abstract

Minichromosome Maintenance Complex Component 2 (MCM2) is a replicative helicase system subunit that is a major prognostic and proliferation marker for gastric, oral, breast, and colon cancers. During the replication procedure, it combines with histones named H3 and H4 by their N-terminal domain to help the assembly and disassembly of nucleosomes on DNA. MCM2 inhibition slows tumor cell growth and causes G0/G1 phase arrest, but it has little effect on cell apoptosis. Due to its complex structural composition and crucial involvement in DNA replication and regulation interface, MCM2 is a potential target for drug discovery. Traditional herbs are gradually gaining popularity. Beneficial functions of phytochemicals include low toxicity, low cost, availability, antioxidant activity, antibacterial action, regulation of detoxification enzymes, regulation of hormones, etc. The signaling pathway of many diseases alters simultaneously, and mutations happen in new ways, due to these reasons, discovering new drug candidates has become badly needed. Through Molecular docking study of compounds, pharmacokinetic property analysis, quantitative structure-activity relationship analysis, and drug-protein interaction against MCM2 protein, this work proposes phytochemical screening of the green tea plant (*Camellia sinensis*) to select the most potential drug compound to inhibit MCM2 protein.

Keywords: MCM2, phytochemicals, *Camellia sinensis*, antioxidant activity, antibacterial action, detoxification enzymes.

I. Introduction

Despite there are several advances in treatment procedures, cancer occupies the first position in global mortality. Effective conventional therapies that lack specificity cause adverse side effects as well as systemic toxicity. This limitation has spurred the pursuit of targeted therapies aimed at specific molecular pathways critical for tumor growth and survival. The Minichromosome Maintenance Complex Component 2 (MCM2) protein has become a promising target. An MCM family member, MCM2 helps build the replication initiation complex[1]. Proteins of 101,896 Da and 904 amino acids are encoded[2]. MCM2 directly binds to DNA replication origins and regulates gene expression to unwind DNA or start replication[3]. MCM2 is the most extensively studied MCMs and is a biomarker for carcinoma diagnosis. High expression of MCM2 is found in solid tumors but is suppressed in normal samples, making MCM2 a potential marker for carcinoma groups. MCM2 is constitutively expressed in, for example, lung cancer tissue samples[4] and ovarian cancer tissue samples, making it a potential therapeutic target[5]. According to these studies, MCM2 knockdown significantly improved ovarian cancer chemoresistance to carboplatin and olaparib. Recent studies have shown that MCM2 is recognized as a key molecule in various cancer-causing genes such as CAMKK2 and MEK1[6].

Plants have served as a foundational source for medicine throughout history, and many contemporary pharmaceuticals are derived from or inspired by plant-based compounds[7,8]. Developing a new drug is complex, often involving high costs and extended timelines, with multiple clinical trials required to ensure safety and efficacy. *Camellia sinensis*, or green tea, is a widely researched plant biochemically rich in epigallocatechin gallate (EGCG), epicatechin, and catechin with antioxidant, anti-inflammatory, and anti-cancer properties. EGCG has been shown to inhibit the growth of cancer cells by modulating key signaling pathways, such as the ones in PI3K/AKT and MAPK pathways[9]. Still, the efficacy of C. sinensisphytocompounds in inhibiting the function of MCM2 protein is untouched.

Previous studies have highlighted the importance of MCM2 as a potential target for therapy. For example, Su(2021) demonstrated that synthetic small molecules can effectively disrupt the MCM2-MCM7 complex, decreasing cancer cell proliferation[10]. Likewise, Wang (2020) recognized MCM2 as a biomarker for cancer progression and a promising target for early treatment. However, there is still a limited exploration of natural products, especially phytocompounds, as MCM2 inhibitors. This gap in the literature is significant, as natural products provide unique benefits, such as structural diversity and lower toxicity[11].

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This research enhances our understanding of natural products in oncology treatment by filling a significant gap in the investigation of C. sinensisphytocompounds as MCM2 inhibitors. In contrast to earlier studies that mainly concentrate on synthetic inhibitors[10,11], our study highlights the importance of natural bioactives in targeting a crucial oncogenic protein. The results could aid in developing safer and more effective cancer treatments, utilizing the pharmacological potential of phytochemicals derived from green tea.

Advances in computational methods, particularly high-throughput virtual screening and rational drug design based on de novo structures, are emerging as valuable tools for streamlining drug discovery[12-14]. Through virtual screening, researchers can identify novel compounds with potential therapeutic applications. This in silico approach has made traditional in vitro screenings more efficient in terms of both time and cost, especially for the discovery of new compounds[15-17].

Two main strategies are employed in virtual screening: ligand-based screening and receptor-based screening. Ligand-based screening identifies candidate compounds by comparing them to known active molecules, while receptor-based screening focuses on finding compounds that interact optimally with a target's binding site, based on its three-dimensional structure[18,19]. In drug lead discovery, molecular modeling is crucial, requiring detailed knowledge of the target protein's three-dimensional structure as well as the configuration of the protein-ligand complex, which forms when the drug binds to its target[20-22].

Various methods, such as pharmacopeia analysis, bioassays, and quantitative structure-activity relationships (QSARs), are also applied to generate new leads or optimize existing compounds[23-25]. Incorporating structure-based drug design into the drug development pipeline enables researchers to discover new molecules with greater efficiency, saving both time and effort compared to traditional methods[26-28].

Studies of pharmacokinetics are an extremely important part of the process of creating new drugs. The time-dependent behavior of medicines and the principal metabolites of those drugs in various body fluids is analyzed as part of these procedures. This gives us a better understanding of the processes of absorption, distribution, metabolism, and elimination of medications from the body. During the Phase I investigations, pharmacokinetically guided dose escalation (PGDE) procedures are used. These tactics are used to help smooth the transition from preclinical research to clinical research. It is impossible to discover and perfect medication therapies without the knowledge that can be gleaned from pharmacokinetics in clinical trials[29-31].

When developing a new drug, it's crucial to consider the chemical properties of the substance being studied at every stage. These properties are known as ADMET, which stands for absorption, distribution, metabolism, excretion, and toxicity. A key goal in drug development is to create compounds that have favorable ADMET characteristics, as these properties determine how the drug will behave in the body[32]. The concept of "drug-likeness" serves as a useful guideline during the early phases of drug creation, helping researchers identify compounds that are more likely to succeed as medications[33].

One of the most widely recognized "drug-likeness" filters was introduced by Lipinski and his colleagues in 1997. This rule, known as Lipinski's Rule of Five, suggests that a compound is more likely to be an effective drug if it meets certain criteria: a molecular weight under 500, an octanol/water partition coefficient (A log P) below 5 (which indicates how well a compound dissolves in fats vs. water), no more than 5 hydrogen bond donors, and no more than 10 hydrogen bond acceptors[34-36].

In another study, Ghose and his team analyzed a large set of chemical compounds. They found that over 80 percent of them met specific requirements, including having a molecular weight between 160 and 480, A log P value ranging from 0.4 to 5.6, a molecular refraction (MR) above 40, and an atom count between 20 and 70[37]. By using these kinds of filters, researchers can streamline the drug discovery process by comparing new compounds to successful drugs based on their physical and chemical properties.

However, it's important to note that some studies have pointed out the limitations of these rules or filters. Relying only on a compound's physical and chemical characteristics doesn't always lead to successful drug development, as there are other factors to consider[38,39].

A great deal of research investigations have shown that consuming green tea can be advantageous in the fight against cancer. Our goal is to improve our understanding of new medicinal product candidates and possible inhibitors against the MCM2 receptor that originates from the leaves of the tea tree by conducting studies in computer simulations.

PyRx may be used to test a compound library for effectiveness against a specific therapeutic target. It is most commonly seen in Computer-Aided Design and Drafting (CADD) design processes. PyRx technologies for molecular docking were utilized, specifically the VinaAutoDock wizard, to locate the protein and ligand binding combinations that were shown to be the most successful[40]. The default setup parameters of the PyRx software were used to determine the docking score (kcal/mol) of ligands. The compounds that had a higher docking score than the control drug were regarded to be "expected drug candidates for the next analysis." At long last, the protein-ligand complex's binding relationship was analyzed and visualized with the help of the software called Discovery Studio[41].

II. Materials & Methods

Preparation of Protein

The 3D experimental tertiary structures of the MCM2 are

presently accessible in the RCSB protein data bank (PDB id: 6XTY) (https://www.rcsb.org/). The PDB structures of the proteins were constructed with the following constraints in mind: human expression, X-ray crystallographic protein structure, elimination of side chains, metal ions, and cofactors, and removal of any cofactors that may have been present. The Chimera software then merged polar and nonpolar hydrogen atoms into a single structure. Concerning the Gasteiger charges that are associated with the system, a decision was reached[42].

Selection of Ligands

Medicines from natural plants contain phytochemicals. These phytochemicals can be used to develop and explore novel medications by covering many chemical areas. Green tea (*Camellia sinensis*) was chosen for its well-known health benefits, which include anti-cancer, antioxidant, and anti-inflammatory properties. The IMPPAT database was an essential tool in identifying these compounds, helping to explore their drug-like characteristics for possible therapeutic uses. Natural product-based medications are identified using the IMPPAT database, which contains around 1742 Indian medicinal plants and 9500 phytochemical compounds[43,44]. AutoDock 4 was used to accurately recognize atoms, connect nonpolar hydrogens, discover aromatic carbons, and form a "torsion tree." In most compound particles, an AD4-like atom is present.

Phytochemicals were selected based on docking results with MCM2. Specifically, the phytochemicals with more docking score than -7.2 kcal/mol were considered for further evaluation. Then the selected phytochemicals were gone through pharmacokinetic property analysis. After that, two phytochemicals that demonstrate decent pharmacokinetic properties were finally selected.

Molecular Docking

Molecular docking, a crucial part of structural biology, is most often used in CADD. This method helps identify which macromolecules will bind to a target macromolecule (such as an enzyme, protein, or drug) in the best way[45,46]. By integrating PyRx virtual screening with AutoDockVina, the molecular docking process was investigated. The need of protein molecular binding energy with the selected phytochemicals was assessed in this investigation.

PyRx is an open-source software used for virtual screening. It can evaluate a library of compounds related to a specific therapeutic target and perform these tasks simultaneously. PyRx is widely used in the CADD process, making it known as CADD software. Its reliability is enhanced by using AutoDock 4 and AutoDockVina as docking tools, along with a simple user interface. PyRx employs molecular docking techniques (using the AutoDockVina tool) to identify the most effective binding configurations between proteins and ligands[47]. The researchers selected the binding configuration with the lowest (most negative) binding energy (in kcal/mol) as the "recommended drug candidate for further trials." This process was completed successfully using PyRx's default settings. Finally, Discovery Studio software was used to visualize the interaction between the protein-ligand complex and the ligand[48].

Pharmacokinetic Property

"PK," or pharmacokinetics, refers to how a drug is processed in the body, including its absorption, distribution, metabolism, and excretion (ADME). In the context of CADD, understanding a drug's ADME properties is critical as it determines how the drug enters and exits the body, how long its effects last, and how it impacts the system overall[49]. These pharmacokinetic characteristics are key to maintaining a drug's stability and effectiveness as a treatment, making them an essential focus during the drug development process.

To explore the early-stage pharmacokinetic features of selected drugs, we used the SwissADME website (http://www.swissadme.ch), a free tool that accurately predicts the ADME properties and drug-likeness of simple compounds. This allowed us to carry out a detailed investigation into these properties. Additionally, we used the PKCSM website (https://biosig.unimelb.edu.au/pkcsm/) to make predictions about the toxicity of the compounds, ensuring a more comprehensive understanding of their safety profiles[50].

Ligand Activity Prediction by QSAR Analysis

The well-established Prediction of Activity Spectra for Substances (PASS) server at http://www.way2drug.com/passonline/ was utilized to compare the two phytochemicals and the control drug. The server predicts outcomes using a substance (PASS) structure. The Simplified Molecular Input Line Entry System (SMILES) format was used to represent the molecular structures of the phytocompounds as well as calculate the corresponding Pa and Pi values for each ligand[51].

III. Results

Molecular Docking Result Analysis

The *Camellia sinensis* (green tea) plant is associated with 248 different phytochemicals that are found in the IMPPAT database. Ligands with a higher docking result that don't satisfy any of the Lipinski, Ghose, Veber, Egan, or Muegge rules are not included in the study. The phytocompounds Quercetin and Luteolin, which are finally recommended, have a docking score of -8.8 kcal/mol. This research used ciprofloxacin as a control ligand since it had previously been found to have an inhibitory effect on the development of cancer cells. The docking score of Ciprofloxacin with MCM2 is -7.2 kcal/mol. The chemicals that have the highest docking scores and the strongest binding affinities are presented in **Table 1**.

Table 1. Chemicals having the highest docking scores

Compound CID	Compound Name	Docking Score (kcal/mol)
CID_5280343 (Quercetin)	Quercetin	-8.8
CID_5280445 (Luteolin)	Luteolin	-8.8
CID_2764 (Control)	Ciprofloxacin	-7.2

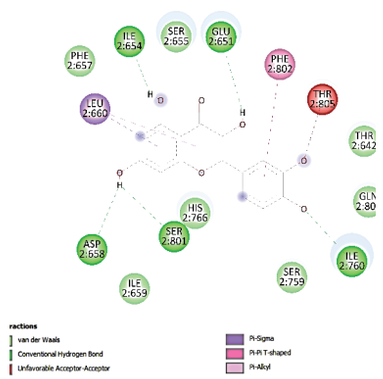
In various biological processes, the interactions between molecules of ligands and proteins are significant and play an important role. Because the idea of molecular complementarity makes it possible, chemical bonding plays an essential part in facilitating these interactions. Interactions between ligands and their targets in proteins ensure precise control over cellular processes. These interactions provide the foundation for the coordination of essential processes that take place inside biological cells. The protein-ligand interaction involving the control medication is depicted in **Table 2**, which contains the compounds that were chosen. **Table 2** displays the different protein-ligand interactions that can occur depending on which ligand is used with the target protein. Conventional hydrogen bonds are shamrock green, van der Waals bonds olive green, carbon hydrogen bonds emerald green, and pi sigma bonds violet in the interaction diagram.

The table highlights the interaction between various compounds and the target protein through the formation of hydrogen bonds, which are crucial in determining the strength and stability of the drug-protein interaction. Specifically, the compound CID_5280343, also known as Quercetin, forms five conventional hydrogen bonds with the target protein. This suggests a strong interaction, as the number of hydrogen bonds can influence how tightly the compound binds to the protein, potentially increasing its effectiveness as a drug candidate.

Table 2. Protein-ligand interaction (ligand used with the target protein)

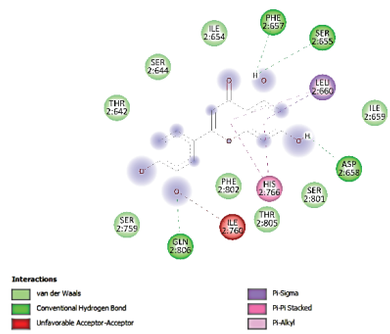
CID_5280343

(Quercetin)



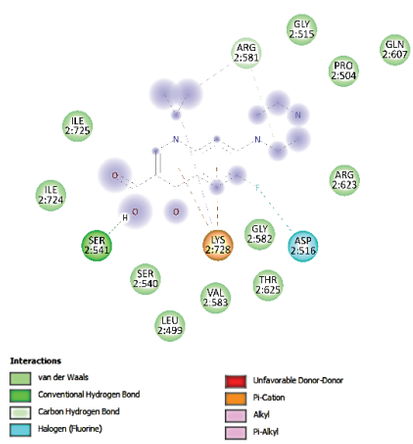
CID_5280445

(Luteolin)



CID_2764

(Control)



In comparison, the compound CID_5280445 (Luteolin) forms four conventional hydrogen bonds with the target protein. While slightly fewer than Quercetin, these compounds still exhibit relatively strong binding interactions. Interestingly, the control drug, CID_2764, which serves as a baseline or standard for comparison in the study, forms only one hydrogen bond with the target protein. This significant difference in the number of hydrogen bonds suggests that the other compounds, particularly Quercetin, may have stronger or more stable interactions with the target protein, potentially making them more effective than the control drug in the context of this study.

Pharmacokinetic and ADME Property Analysis

Table 3 illustrates the fundamental physiochemical characteristics of the chosen medicinal molecule. Because breaking these rules leads to issues with bioavailability, every one of the chosen ligands abides with Lipinski, Ghose, Veber, Egan, and Muegge's rules.

Molecular weight: the lower it is, the better because diffusion is directly influenced by it. The molecular weights of the vast majority of medications currently available on the market range anywhere from 200 to 600 Daltons. They are considered to be part of the class of relatively tiny molecules.

Luteolin has a lower molecular weight than the other compounds included in table 3. The total amount of atoms in a molecule that are not hydrogen is referred to as the heavy atom count. According to Lipinski's definition of a drug, the total number of heavy atoms in a compound must be equal to or fewer than 36 for that substance to be deemed a valid substance.

Table 3. Physiochemical properties of the selected compounds

Compound CID	Formula	Molecular weight (g/mol)	Number of heavy atoms	Number of heavy aromatic atoms	Fraction Csp3	Number of H-bond donors	Number of H-bond acceptors	Number of rotatable bonds	Molar Refractivity
CID_5280343 (Quercetin)	C15H10O7	302.24	22	16	0	5	7	1	78.03
CID_5280445 (Luteolin)	C15H10O6	286.24	21	16	0	4	6	1	76.01
CID_2764 (Control)	C17H18 FN3O3	331.34	24	10	0.41	2	5	3	95.25

All values that are shown in **Table 3** are convenient. For instance, a drug compound should contain 36 or fewer heavy atoms, which is rooted in practical factors related to drug-likeness and pharmacokinetics. All values of total heavy atoms of recommended compounds are under 36.

Moreover, one description of a rotatable bond is any single bond that is not part of a ring and that is bonded to an atom that is not the terminal or a hydrogen atom. Another definition of a rotatable bond is any bond that may be broken and reformed into its original form. The number of rotatable bonds must be lower than three to fulfill the requirements.

In this scenario, not a single one of the compounds possesses a value greater than 3, but everyone has a value less than 3. When it comes to molar refractivity, the acceptable range is someplace in the area of 40 and 130. At least one location within this range contains each of the values.

Table 4. Absorption properties of the selected ligands

Compound CID	Water solubility [log mol/L]	$CaCO_2$ permeability [log Papp in 10^{-6} cm/s]	Intestinal absorption (human) [% Absorbed]	Skin Permeability [log Kp]	P-glycoprotein substrate	P-glycoprotein I inhibitor	P-glycoprotein II inhibitor
CID_5280343 (Quercetin)	-3.047	0.294	70.277	-2.737	Yes	No	No
CID_5280445 (Luteolin)	-3.094	0.096	81.130	-2.735	Yes	No	No
CID_2764 (Control)	-2.897	0.492	96.466	-2.734	Yes	No	No

The ligands' absorption properties can be forecasted using **Table 4**, which contains all of the relevant information. When a drug ingredient can be dissolved in 250 milliliters of solution at its greatest concentration, we refer to this property as "high solubility." The values of water solubility are presented in the log scale in the table 4 that can be found here. After going over the results, we can conclude that they have an extremely high solubility in water. It is recommended that

the $CaCO_2$ permeability be more than 5 x 10^{-6} cm/s. The value when converted to logarithms is -5.30. The table contains no values that are lower than -5.30.

Table 5. Distribution properties of the selected ligands

Compound CID	VDss (Human) (log L/kg)	Fraction unbound (human) Numeric (Fu)	BBB permeability (log BB)	CNS permeability (log PS)	Total Clearance (log ml/min/kg)	Renal OCT2 substrate
CID_5280343 (Quercetin)	0.746	0.118	-0.719	-2.976	0.044	No
CID_5280445 (Luteolin)	1.153	0.168	-0.907	-2.251	0.495	No
CID_2764 (Control)	-0.17	0.648	-0.587	-2.999	0.633	No

These compounds are ideal candidates for use as therapeutic compounds due to the high $CaCO_2$ permeability that they exhibit. High intestinal absorption might range anywhere from 80 to 100 percent. Quercetin has a medium intestine absorption capability, while Liteolin has a high intestinal absorption capability. Based on the data presented in **Table 5**, it is possible to deduce that the drugs that have been suggested do not contain a renal oct2 substrate, and the value of the total clearance falls within a range that is considered acceptable.

Table 6. Metabolism properties of the selected ligands

Compound CID	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor
CID_5280343 (Quercetin)	No	No	No	No	No	No	No
CID_5280445 (Luteolin)	No	No	Yes	No	Yes	No	No
CID_2764 (Control)	No	No	No	No	No	No	No

The use of any of these inhibitors that were shown in Table 6 may have hazardous effects. Pharmaceuticals that, upon metabolism, produce active metabolites that tend to reduce the effectiveness of the medicine in question.

Table 7. Toxicity properties of the selected ligands

Compound CID	AMES toxicity	Max. tolerated dose (human) (log mg/kg/day)	hERG I inhibitor	hERG II inhibitor	Oral Rat Acute Toxicity (LD50) (mol/kg)	Oral Rat Chronic Toxicity (LOAEL) (log mg/kg_bw/day)	Hepatotoxicity	Skin Sensitisation	T.Pyriformis toxicity (log ug/L)	Minnow toxicity (log mM)
CID_5280343 (Quercetin)	No	0.25	No	No	2.042	2.605	No	No	0.39	2.305
CID_5280445 (Luteolin)	No	0.499	No	No	2.455	2.409	No	No	0.326	3.169
CID_2764 (Control)	No	0.924	No	No	2.891	1.036	Yes	No	0.286	1.194

It is clear from looking at **Table 7** of the toxicology report that none of the compounds demonstrated any toxicity against AMES. The phytocompounds that we chose to study do not have any inhibitory effect on hERG II.

For pharmacological risk management, an understanding of the acute oral toxicity of medication in rats is vital. It is common practice to quantify this toxicity using the term "50% lethal dose," or "LD50." This term refers to the amount

of the chemical that is anticipated to result in the death of fifty percent of the animals treated over a predetermined duration of time. When compared to the drug that served as the standard of comparison, the phytochemicals that we recommend have a reduced level of acute toxicity when administered orally to rats. The phytochemicals that have been suggested will not result in skin sensitivity. In contrast to the hepatotoxicity exhibited by Ciprofloxacin, the in-silico analysis forecasts that the phytochemicals under consideration will not exhibit any hepatotoxic effects.

PASS Online Prediction for QSAR Analysis

Two phytochemicals and a placebo were tested using the PASS online program to see whether they had any chance of blocking of the MCM2 protein tyrosine kinase domain. Higher Pa values are associated with compounds that have more pharmacological potency and potential for experimental synthesis. We utilized a Pa cut-off value of 100 to investigate the QSAR of these two phytochemicals and the control medication. Even though it cannot forecast binding affinity for novel therapeutic targets, PASS can nevertheless help minimize the negative effects of a compound. The ADME evaluation was followed by a site-specific molecular docking study of the filtered phytochemicals. These values are shown in **Table 8**.

IV. Discussion

In every region of the world, cancer is the top cause of mortality. There has been a discernible rise in the number of cases of cancer in recent years. Because of this, the investigation of mutations in the MCM2 gene is of significant importance. CADD is a particularly useful tool for locating novel compounds that target particular proteins because it incorporates a wide variety of and a high level of sophistication in its capabilities and procedures. The overall goal of the CADD approach is to reduce the financial expenditures as well as the time restrictions that are connected with the developing procedure of new drugs. The approach of virtual screening was developed to use a wide variety of computational approaches, including molecular docking, quantum mechanics, ADMET, and other relevant methodologies. Research & development in the pharmaceutical industry places a significant emphasis on the inclusion of this specific component.

The purpose of this study was to ascertain the existence of the MCM2 protein as well as its properties and to assess the efficacy of several medication candidates by utilizing molecular docking and other experimental methods. The compounds were evaluated using a technique known as molecular docking during the first step of the process. Following that, two phytocompounds were chosen because of their better negative binding affinity in comparison to the control ligand, which was ciprofloxacin. The chosen phytochemicals had docking scores that are higher when compared to ciprofloxacin, which is being already introduced as a medicinal drug for the treatment of cancer in human patients. Following that comes the examination of the pharmacokinetic and QSAR features. The chemicals that we selected to study produced favorable outcomes across the board for this investigation.

V. Conclusion

CID_5280343 and CID_5280445 are some of the most promising potential MCM2 protein antagonists in the case of human malignancies. These compounds have been selected based on their good predicted pharmacokinetics and results of the analyses in QSAR studies making them ideal for this purpose. This experiment will also try to evaluate the usefulness of these agents for human cancer immunotherapy, raising new ways to treat cancer. The next stage includes laboratory studies (both in vitro and in vivo) intended to assess the anticancer efficacy of these phytochemicals and their safety. Even though the obtained results from the evaluation are encouraging, preclinical studies using animals have to be performed to conclusively establish the efficacy and possible safety of the phytochemicals. In cell lines and animals, their MCM2 protein inhibitory activities, tumoricidal activities, and toxic side effects will be screened. This phase is important as, in biological systems, there are complex relationships that cannot be fully created in silico. Furthermore, these studies will help to find the appropriate dose and enhance the compounds for efficacy and safety. The overriding goal is to create an enabling environment for clinical studies and in the end, provide treatments for cancer that are natural, targeted, and inexpensive.

Table 8. Prediction of QSAR Analysis

CID	Compounds name	Pa	Pi	Activity
5280343	Quercetin	930	1	CYP1A1 inducer
		931	2	UGT1A9 substrate
		933	1	MAP kinase stimulant
		934	1	Quercetin 2,3-dioxygenase inhibitor
		938	3	Membrane permeability inhibitor
		939	2	UGT1A10 substrate
		940	3	CYP1A1 substrate
		940	1	Antimutagenic
		945	4	CYP1A substrate
		944	2	UGT1A6 substrate
		951	1	CYP1A inducer
		957	2	HMOX1 expression enhancer
		962	1	Peroxidase inhibitor
		969	2	HIF1A expression inhibitor
		973	2	Membrane integrity agonist
		927	1	NADPH-ferrihemoprotein reductase inhibitor
5280445	Luteolin	932	2	CYP1A inducer
		935	2	HMOX1 expression enhancer
		936	2	Peroxidase inhibitor
		942	5	CYP2C12 substrate
		940	2	Kinase inhibitor
		940	1	Antimutagenic
		942	1	P-benzoquinone reductase (NADPH) inhibitor
5280445	Luteolin	947	3	Aldehyde oxidase inhibitor
		947	1	Aryl-alcohol dehydrogenase (NADP+) inhibitor
		952	2	2-Dehydropantoate 2-reductase inhibitor
		953	2	Membrane permeability inhibitor
		964	3	HIF1A expression inhibitor
		965	3	Membrane integrity agonist
		978	1	Chlordecone reductase inhibitor
2764 (Control)	Ciprofloxacin	452	19	Antituberculosis
		546	103	Nootropic
		448	4	Antiviral (CMV)
		468	1	DNA gyrase inhibitor
		576	97	Antieczematic
		505	10	RELA expression inhibitor
		567	1	Antibiotic Quinolone-like
		588	9	Antibacterial
		595	6	Antiamyloidogenic
		638	35	Glutamate-5-semialdehyde dehydrogenase inhibitor
		639	8	Antimycobacterial
		751	3	Topoisomerase II inhibitor
		786	4	DNA synthesis inhibitor
		823	5	Antiinfective
		909	0	Antibacterial, ophthalmic

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