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***Corresponding author:**
Dr. P Ravikumar
Head & Project Coordinator, Iyarvi Research Center for Bioinformatics (IRCB), Erode, Tamil Nadu, India
Email: headircb@gmail.com

Finding Focal Adhesion Kinase Inhibitors from Indian Medicinal Plants for Colorectal Cancer- An *In-silico* Approach

P Srivedha[1], V Umabarathi[2], BM Muhilan[2], P Ravikumar[2]

[1]Department of Biotechnology & Bioinformatics, Bishop Heber College (Autonomous), Tiruchirappalli, Tamil Nadu, India

[2]Iyarvi Research Center for Bioinformatics (IRCB), Erode, Tamil Nadu, India

ABSTRACT

Colorectal cancer is one of the most frequent malignancies worldwide. An uncontrolled growth of the body's cells can lead to cancer. Cancer of the large intestine (colon) is one of the main causes of death due to cancer. The present study was designed to find the potential phytocompounds from Indian medicinal plants against Colorectal cancer (CRC) using *in silico* studies. The 3D structure of the target protein was retrieved from the PDB database. The 3D structure of phytocompounds was obtained using IMPPAT, PubChem and Dr. Duke's database. The Lipinski rule of five for all the phytocompounds was tested using SwissADME. The docking studies were performed using PyRx, and the results were analyzed using Discovery Studio 2021. From the results, the phytocompounds Pamoic acid, Fernenol, and Diosgenin showed very good binding affinity like -9.7, -9.4, and -9.1 Kcal/mol, respectively. Toxicity studies were done for the best-interacted phytocompounds, and the results showed that the compounds had very less toxicity. The present study concludes that Pamoic acid from *Catharanthus roseus*, Fernenol from *Artemisia vulgaris*, and Diosgenin from *Solanum nigrum* has the potential ability to act as a drug for treating colorectal cancer (CRC).

Keywords: Colorectal cancer, Medicinal plants, Phytocompounds, Molecular docking, PyRx, Drug discovery.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common cancers globally, with males and females having the second and third most cases, respectively, and males and females having the fourth and third most cancer-related deaths [1].

Furthermore, despite all of modern medicine's efforts, the prognosis of CRC patients is mostly determined by the stage of the disease at the time of diagnosis [2]. Although it is generally understood that early discovery of CRC reduces associated mortality and that early detection of its precursor lesion can even reduce the occurrence, current CRC screening regimens still have several limitations [3].

Colorectal cancer (CRC) is the fourth most frequent cancer worldwide, accounting for 9.7% of all cancer deaths [4, 5]. It affects 746,000 males (or 10% of all cancer cases) and 614,000 women (or 9.2% of all cancer cases), with the majority of cases (55%) happening in industrialized countries [5, 6]. Furthermore, 42,300 new cases of colorectal cancer are identified in the United Kingdom each year, making it the fourth most prevalent disease overall and the third most common in both men and women [5]. Moreover, between 1991 and 2016, the incidence of colorectal cancer increased, owing to changes in lifestyle, environmental factors, and the ageing population [7, 8]. Although the incidence of colon cancer has decreased by 4% in the UK over the last decade, lifestyle risk factors persist. However, by 2030, the worldwide burden of CRC is predicted to rise, with 2.2 million additional cases and 1.1 million fatalities expected [9]. Furthermore, managing disease burden poses substantial obstacles. The five-year overall survival rate for CRC in England is 58.4 percent, which is lower than the 60–65 percent reported in the United States. Conversely, between 1996 and 2014, the US stated survival rate remained constant [10, 11]. The ageing population and advanced illness presentation pose additional concerns [12]. Patients over 75 years old account for 44% of new colorectal cancer diagnoses, while an estimated 20–25% of CRC patients are identified at a metastatic stage, with another 25% developing metastases throughout their disease [5-11]. As a result, CRC is responsible for 8.5 percent of cancer-related fatalities worldwide, with 16,300 deaths per year in the United Kingdom, making it the second leading cause of cancer-related deaths at 10%. Despite the fact that survival varies by stage, with 92 percent survival for stage I compared to 10% for stage IV, there has been an improvement in survival for the 60–69 year age group due to screening [5]. As a result, CRC remains a common problem in cancer treatment, stressing the importance of early detection.

Colorectal cancer usually originates as a polyp in the intestinal walls and targets the large intestine. In the United States, colorectal cancer is the leading cause of cancer-related death [13]. Colorectal cancer can affect both men and women equally, however males are more commonly impacted than women, and it is the second most commonly diagnosed cancer after lung cancer [14]. When it comes to colorectal cancer, the problem is that the signs and symptoms are difficult to identify, and the alarming signs and symptoms are usually recognized at later stages, when metastasis has already begun, and the survival rate has dropped to 10–15 percent [15]. Blood in the stool and difficulty while passing the colon are two of the most prevalent signs of colorectal cancer, which are followed by inflammation and pain in the abdomen [16]. When it comes to tumor location in the colon, the adenoma or polyp is most commonly seen where the blood supply enters the intestinal wall, which has a variety of consequences in research and therapy [17]. Cancer takes 5–10 years to grow and spreads mostly through the blood and lymphatic system. Because blood travels immediately to the liver, followed by the lungs and bones, the liver is a popular site for metastatic cancer to spread [18].

Chemotherapy is used to treat both early-stage and metastatic cancer patients, with the conventional method consisting of surgery supplemented with radiotherapy and/or chemotherapy (depending on tumor site and progression of disease) [19, 20]. The chemotherapy backbones for treating metastatic CRC are fluoropyrimidines (such as 5-fluorouracil, 5-FU), oxaliplatin, and irinotecan, and their sequential administration provides for median overall survival of 18 to 20 months [21]. The barrier to effective clinical outcomes for CRC patients is recurrence following chemotherapy.

According to the National Cancer Institute, oxaliplatin is the only metal-based medication now used for CC that has been approved by the Food and Drug Administration (FDA) [22]. Oxaliplatin is frequently given intravenously (i.v.) in conjunction with other anticancer medications such 5-fluorouracil (5-FU) or capecitabine [23]. The toxicity of metallodrugs, such as nephrotoxicity, myelotoxicity, ototoxicity, neurotoxicity, nausea, and vomiting [24-26].

In *in vitro* and *in vivo* investigations, green tea leaves with high catechin levels promoted apoptosis in colon cancer cells and reduced the production of the vascular endothelial growth factor (VEGF) and its promoter activity. When compared to the control group, the extract boosted apoptosis (programmed cell death) by 1.9 times in cancer cells and 3 times in endothelial cells [27]. In this investigation, garlic was also an effective herb. Allicin and organosulfur compounds are found in its roots. They reduced cancer cell proliferation and triggered death in an *in vitro* research by inhibiting the phosphoinositide 3-kinase/Akt pathway [28]. S-allylcysteine and S-allylmercaptocysteine, both found in garlic roots, have anticancer effects. *In vitro* research on olive fruit revealed that the presence of 73.25 percent maslinic acid and 25.75 percent oleanolic acid can enhance peroxide anions in the mitochondria of HT-29 cancer cells. It also causes programmed cell death via the internal pathway by increasing caspase 3-like activity by up to 6 times [29].

FAK (Focal Adhesion Kinase) is a non-receptor tyrosine kinase that is localized to cellular focal adhesions and is a key integrin-dependent tyrosine phosphorylated protein [30]. Although several researches have been done on the involvement of FAK with breast cancer, its link to CRC has just recently been discovered. FAK, or protein tyrosine kinase 2, is linked to Src kinase and other tyrosine kinases [31]. FAK structural interactions with numerous kinases may be linked to cancer development, survival, and metastasis. The Src kinase interacts directly with the cytoplasmic domain of the integrin to activate FAK [32].

In the present study, Nine Indian medicinal plants such as *Artocarpus hirsutus* [33], *Artemisia vulgaris, Solanum nigrum* [34], *Asclepias curassavica linn* [35], *Catharanthus roseus, Emblica officinalis* [36], *Cuscuta reflexa* [37], *Coriandrum sativum* [38], and *Tinospora cordifolia* [39] were taken to find the potential inhibitors for Focal Adhesion Kinase of Colorectal cancer.

MATERIALS AND METHODS

Ligand selection

Using literature, IMPPAT (Indian Medicinal Plants, Phytochemistry and Therapeutics) database [40] and Dr duke's database [41] around the 675 phytochemical compounds were selected from the different Indian medicinal plants like *Artocarpus hirsutus* [33], *Artemisia vulgaris, Solanum nigrum* [34], *Asclepias curassavica linn* [35], *Catharanthus roseus, Emblica officinalis* [36], *Cuscuta reflexa* [37], *Coriandrum sativum* [38], and *Tinospora cordifolia* [39] for treating Colorectal cancer. The 3D structure of these compounds was retrieved from the PubChem database [42] and using SwissADME [43] they were subjected to test Lipinski Rule of Five. From the results, 564 compounds obeyed Lipinski Rule of Five and these compounds were taken for the study.

Target protein selection and preparation

The target protein Focal Adhesion Kinase (FAK) belonging to PTK2 gene was found in the literature for CRC [44]. FAK is a major integrin-dependent tyrosine phosphorylated protein, recently, FAK association with colorectal cancer (CRC) has gained attention. The various cancer-promoting mechanisms that associated with FAK can be implicated in the progression of CRC was found in the literature for CRC [45].

The UniProt ID of this target protein was taken from the UniProt database [46]. The 3D structure of this target protein was retrieved from the PDB (Protein data bank) database [47].

Docking studies

Docking studies for the target protein Focal Adhesion Kinase (FAK) and the phytocompounds (ligands) were done using PyRx 0.8 software [48]. The target protein was further prepared for docking studies using this software. All the ligands were uploaded using Open Babel option in the PyRx 0.8. The grid was generated and the docking studies were performed using Vina wizard option in the PyRx 0.8. The values of binding affinity were saved in XL file. The results were analyzed using Discovery Studio 2021 and the 2D and 3D docked images were taken. In the results, the lowest binding affinity indicates good result.

ADMET and CYP properties

ADMET (Adsorption, Distribution, Metabolism, Excretion, and Toxicity) and CYP (Cytochrome P450) properties were tested for all the best-interacted phytocompounds using SwissADME [43]. Lipinski, BBB (Blood - Brain Barrier), HIA (Human Intestinal Absorption), PGP (P-

glycoprotein), XLogP3, TPSA (Topological Polar Surface Area), LogS, Fraction Csp3, Rotatable bonds, CYP enzyme inhibitor properties, Skin permeation and ABS (A Bioavailability Score) were evaluated for all the best-interacted compounds.

RESULTS

Ligand and Target protein selection

The 3D structure of ligands (phytocompounds) was retrieved from the PubChem database. The 3D structure of the target protein Focal Adhesion Kinase (FAK) was obtained from PDB database and its PDB ID is 1MP8. The 3D structure of the target protein is shown in Figure 1.

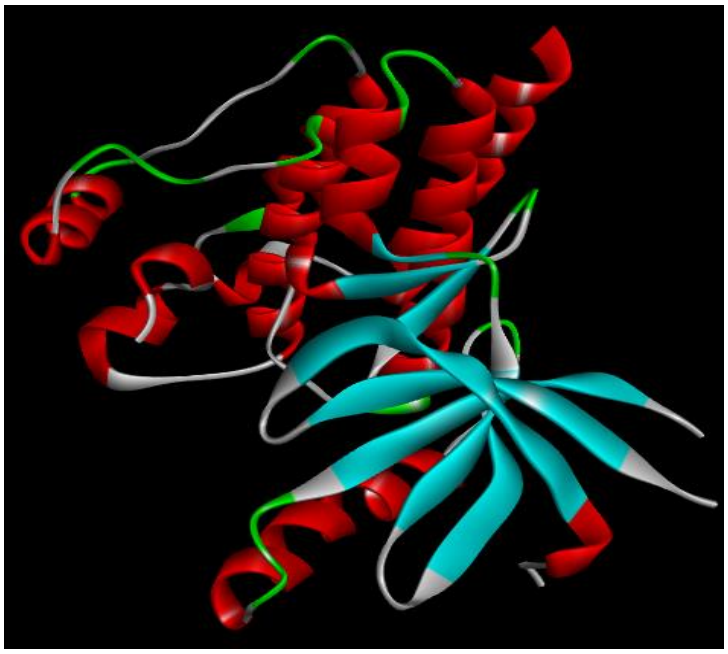

Figure 1: The 3D structure of Target protein FAK

Docking studies

Docking studies for the target protein Focal Adhesion Kinase (FAK) and the phytocompounds (ligands) were done using PyRx 0.8 software. In the results, the following 10 phytocompounds showed very good interaction with the target protein and the results are showed in Table 1. The 2D and 3D interaction of phytocompounds and synthetic drug with the target protein are shown in Figure 2-9.

Table 1: Interaction of Phytocompounds with the target protein

S. No.	PubChem (CID)	Compound Name	Plant Name	Binding Affinity (Kcal/mol)	No. of Bonds	Interacting Residues	Bond Length (Å)
1.	8546	Pamoic acid	*Catharanthus roseus*	-9.7	14	LEU 553 LEU 553 LEU 553 GLU 506 GLU 506 GLU 506 GLU 430 VAL 436 VAL 436 ALA 452 CYS 502 ILE 428 ILE 428 ILE 428	3.57 3.95 3.97 2.22 2.94 2.18 2.71 5.42 5.12 4.09 5.25 3.88 2.58 2.60
2.	12305178	Fernenol	*Artemisia vulgaris*	-9.4	5	ILE 428 VAL 436 ALA 452 CYS 502 LEU 553	5.20 5.31 4.35 5.45 4.40

3.	99474	Diosgenin	*Solanum nigrum*	-9.1	6	LEU 553 LEU 553 CYS 503 ALA 452 VAL 436 VAL 436	4.27 4.53 1.14 4.08 5.02 5.46
4.	5281855	Ellagic acid	*Phyllanthus emblica (officinalis)*	-9	16	GLU 506 LEU 553 LEU 553 LEU 553 ILE 428 ILE 428 VAL 436 VAL 436 VAL 436 VAL 436 ALA 452 ALA 452 GLU 500 LYS 454 LYS 454 LYS 454	2.10 3.60 5.46 3.97 1.97 5.35 4.60 5.19 4.12 4.16 4.10 5.36 1.87 5.13 2.74 2.78
5.	73170	Alpha-Amyrin	*Artemisia vulgaris*	-9	3	LEU 553 ALA 452 VAL 436	4.43 5.17 4.73
6.	5280619	4,21-Dehydrogeissoschizine	*Catharanthus roseus*	-8.9	7	GLU 506 VAL 436 ALA 452 ALA 452 CYS 502 LEU 553 LEU 553 LEU 553 ASP 564 ASP 564 LYS 454	3.25 3.87 3.96 5.05 5.05 4.69 4.86 3.60 2.47 3.07 2.36
7.	5385014	Pleiocarpamine	*Catharanthus roseus*	-8.9	13	 GLU 506 VAL 436 ALA 452 MET 499 VAL 484 ASP 564 ASP 564 LYS 454 LYS 454 LYS 454 LEU 553 LEU 553 LEU 553	3.36 4.34 4.74 4.83 5.16 2.11 3.71 2.87 5.00 4.98 4.63 5.32 3.81
8.	293754	Amyrin acetate	*Catharanthus roseus*	-8.8	3	LEU 553 ALA 452 VAL 436	4.54 4.79 4.60
9.	107985	Triptolide	*Catharanthus roseus*	-8.6	4	CYS 502 ASP 564 LYS 454 GLY 431	1.76 3.29 1.86 3.51
10.	78358538	Vindolinine. 19-epimer, N-oxidess.	*Catharanthus roseus*	-8.6	5	LEU 553 ILE 428 VAL 436 LYS 454 LYS 454	3.85 4.90 5.42 3.08 5.27

SYNTHETIC DRUG							
11.	31703	Adriamycin	--	-8.5	10	GLN 432	2.28
						LYS 454	1.93
						ALA 452	4.49
						CYS 502	5.28
						ILE 428	3.72
						ILE 428	3.72
						LEU 553	3.77
						LEU 553	4.35
						GLU 506	2.68
						GLU 430	3.42

From the results (Table 1), among other compounds, 10 compounds had the best results with the target protein. In which, the phytocompound Pamoic acid showed the best binding affinity (-9.7 Kcal/mol) with the following amino acid residues LEU 553, GLU 506, GLU 430, VAL 436, ALA 452, CYS 502, ILE 428, and ILE 428 of the target protein. The phytocompound Fernenol also showed very good binding affinity of -9.4 Kcal/mol with the amino acid residues ILE 428, VAL 436, ALA 452, CYS 502 and LEU 553. The binding affinity -9.1 Kcal/mol of the phytocompound Diosgenin and the amino acid residues LEU 553, CYS 503, ALA 452, and VAL 436 of target protein. Out of other compounds, the phytocompound Vindolinine. 19-epimer, N-oxidess results the lowest binding affinity (-8.6 Kcal/mol) along the amino acid residues LEU 553, ILE 428, VAL 436, and LYS 454 of target protein. Besides, the binding affinity of the Synthetic drug Adriamycin with the target protein was -8.5 Kcal/mol and the interacted the amino acid residues were GLN 432, LYS 454, ALA 452, CYS 502, ILE 428, LEU 553, GLU 506 and GLU 430.

Thus, in the results of the present study, all the phytocompounds showed the best binding affinity when compared to the Synthetic drug Adriamycin. In which, the phytocompounds Pamoic acid, Fernenol and Diosgenin showed the highest binding affinity among the other phytocompounds.

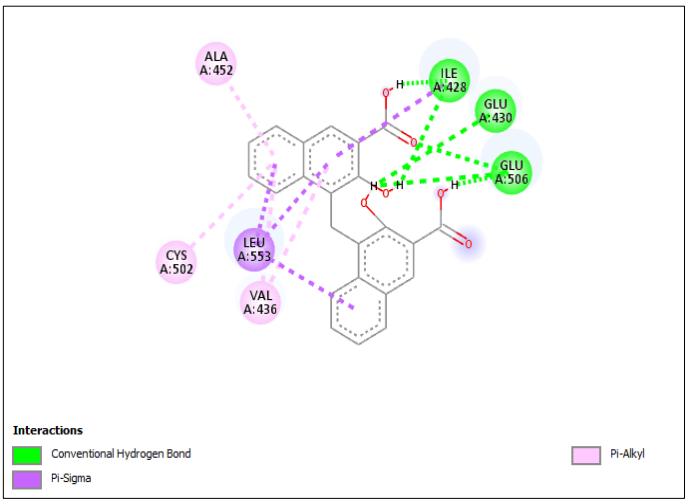

Figure 2: The 2D interaction of phytocompound Pamoic acid with the target protein

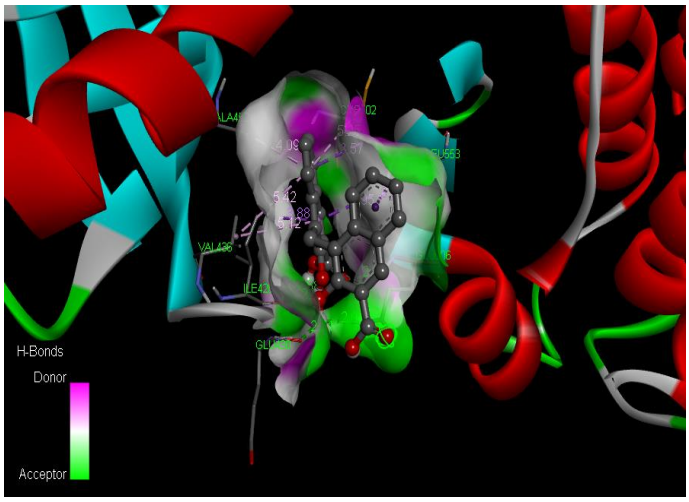

Figure 3: The 3D interaction of phytocompound Pamoic acid with the target protein

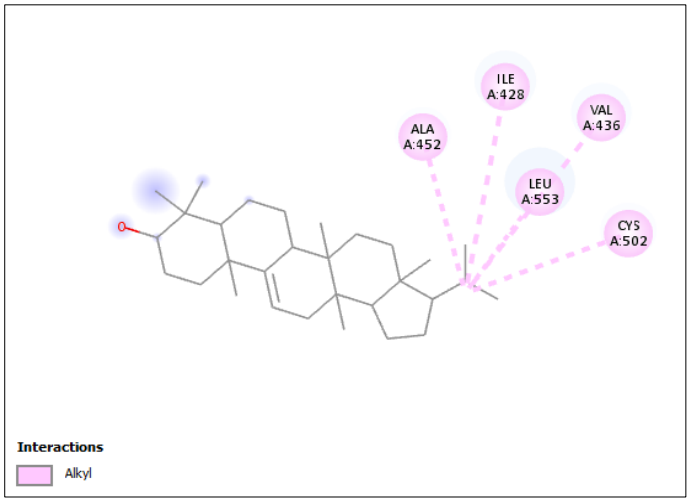

Figure 4: The 2D interaction of phytocompound Fernenol with the target protein

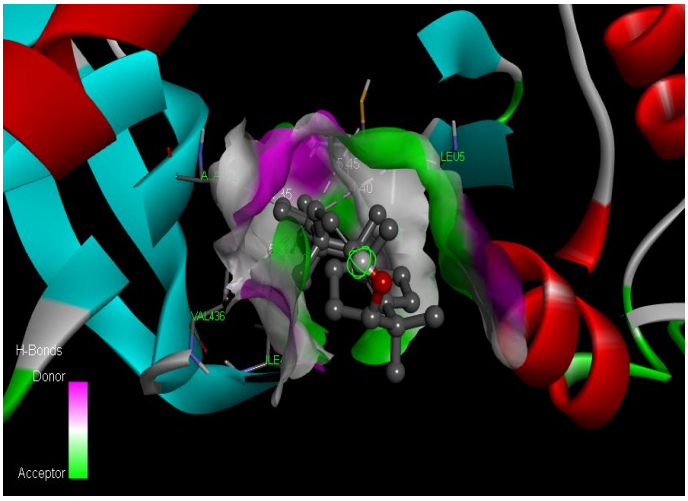

Figure 5: The 3D interaction of phytocompound Fernenol with the target protein.

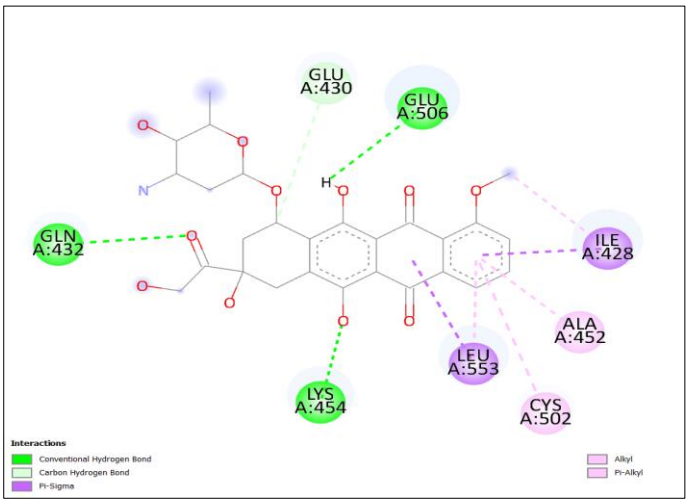

Figure 8: The 2D interaction of synthetic drug Adriamycin with the target protein

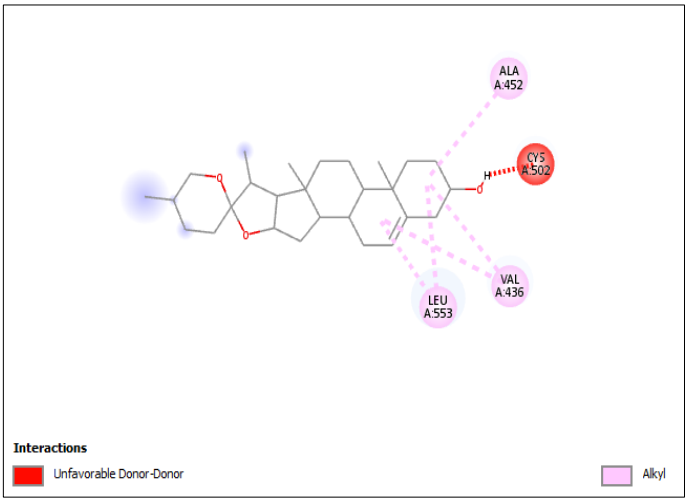

Figure 6: The 2D interaction of phytocompound Diosgenin with the target protein

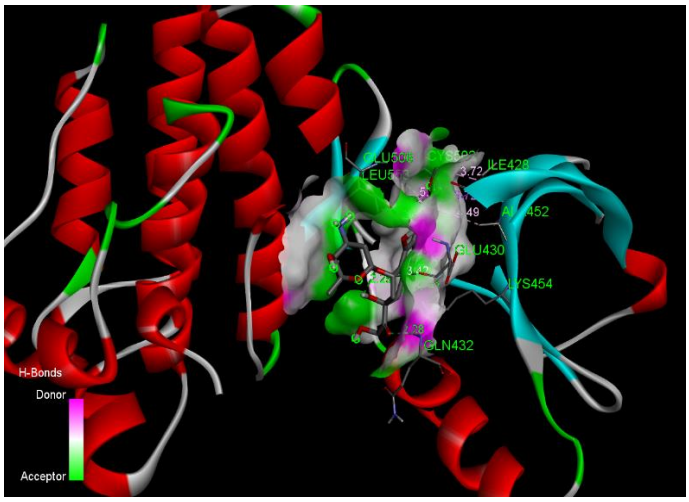

Figure 9: The 3D interaction of synthetic drug Adriamycin with the target protein

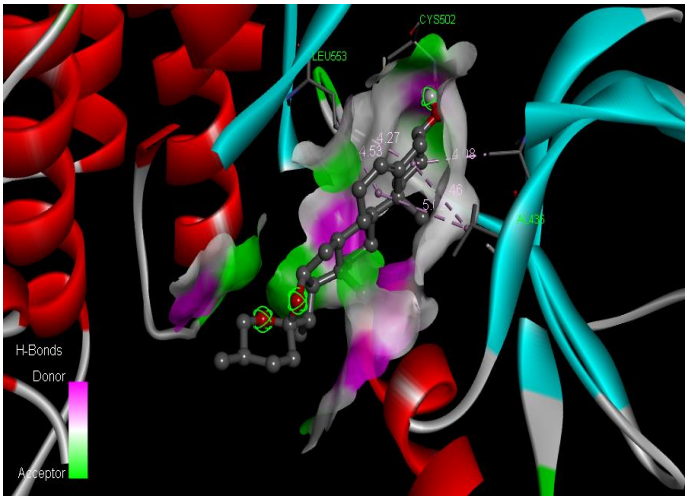

Figure 7: The 3D interaction of phytocompound Diosgenin with the target protein

ADMET and CYP Properties

In the present study, ADMET properties were tested for the best interacted phytocompounds and Synthetic drug Adriamycin using SwissADME and the results were tabulated (Table 2). From the results, all the best interacted phytocompounds obey Lipinski rule of five but Synthetic drug Adriamycin did not obey Lipinski rule. Most of the compounds did not cross Blood – Brain Barrier (BBB) and had high Intestinal Absorption (HIA). Many phytocompounds predicted to be effluated from the CNS by P-glycoprotein. Among the 10 compounds, XLogP3 value of 5 compounds were within the range. TPSA (Topological Polar Surface Area) and Log S value of the most of the compounds were within the limit. In all the compounds, Fraction Csp3 value of 2 compounds were less than 0.25 and the value of other compounds were above this limit. Rotatable bonds for most of the compounds were within the limit.

From the results of the Boiled Egg image of the phytocompounds (Figure 10), the compounds Diosgenin (PubChem CID: 99474), Pleiocarpamine (PubChem CID: 5385014), 4,21-Dehydrogeissoschizine (PubChem CID: 5280619) and Vindolinine. 19-epimer, N-oxide. (PubChem CID: 78358538) are located in the Egg-yolk region, which

means the compounds are passively absorbed by the gastrointestinal tract and can also permeate through the blood-brain barrier. And the compounds Triptolide (PubChem CID: 107985), Pamoic acid (PubChem CID: 8546) and Ellagic acid (PubChem CID: 5281855) are located Egg-white region, which means they are passively absorbed by the gastrointestinal tract but cannot permeate through the blood brain barrier. Moreover, the compounds Diosgenin, Pleiocarpamine, Pamoic acid and Ellagic acid are predicted not to be effluated from the central nervous system by the P-glycoprotein. And the compounds 4,21 – Dehydrogeissoschizine, Vindolinine. 19-epimer, N-oxide and Triptolide are predicted to be effluated from the central nervous system by the P-glycoprotein.

In the results of CYP properties, (Table 3) most of the compounds does not inhibit the CYP450 enzymes and does not give any adverse reactions. Ellagic acid inhibits CYP1A2, Further, Pleiocarpamine and Vindolinine. 19-epimer, N-oxide inhibits CYP2D6 enzymes, respectively. The value of log K_p (Skin Permeant) is good for all compounds and ABS is good for 8 compounds out of 10.

From the results (Table 3), the following compounds Pamoic acid, Fernenol, Diosgenin, Alpha-Amyrin, 4,21-Dehydrogeissoschizine, Amyrin Acetate and Triptolide did not inhibit any CYP450 enzymes. The compound Ellagic acid inhibited only one CYP1A2 enzymes also, compounds like Pleiocarpamineand Vindolinine. 19-epimer, N-oxide inhibited CYP2D6 respectively. Whereas synthetic drug Adriamycin, ABS score is 0.17 means it fails the rule of five.

Table 2: ADMET Properties of Phytocompounds

S. No	PubChem (CID)	Compound Name	Lipinski	BBB	HIA	PGP-	XLOGP3	TPSA (Å)	Log S (ESOL)	Fraction Csp3	Rotatable Bonds
1.	8546	Pamoic acid	Yes	No	High	Yes	5.79	115.06	-6.14	0.04	4
2.	12305178	Fernenol	Yes	No	Low	NA	9.01	20.23	-8.10	0.93	1
3.	99474	Diosgenin	Yes	Yes	High	Yes	5.67	38.69	-5.98	0.93	0
4.	5281855	Ellagic acid	Yes	No	High	Yes	1.10	141.34	-2.94	0.00	0
5.	73170	Alpha-Amyrin	Yes	No	Low	NA	9.01	20.23	-8.16	0.93	0
6.	5280619	4,21-Dehydrogeissoschizine	Yes	Yes	High	No	2.69	65.33	-3.77	0.33	3
7.	5385014	Pleiocarpamine	Yes	Yes	High	Yes	2.45	34.47	-3.53	0.45	2
8.	293754	Amyrin acetate	Yes	No	Low	NA	9.58	26.30	-8.65	0.91	2
9.	107985	Triptolide	Yes	No	High	No	0.22	84.12	-2.15	0.85	1
10.	78358538	Vindolinine. 19-epimer, N-oxide.	Yes	Yes	High	No	2.44	67.76	-3.60	0.57	2
Synthetic drug											
11.	31703	Adriamycin	No	No	Low	NA	1.27	206.07	-3.91	0.44	5

Note: Obey Lipinski: Yes means 0 violation and good, BBB (Blood - Brain Barrier): Yes means good, HIA (Human Intestinal Absorption): High means good, PGP- (Molecules predicted not to be effluated from the CNS by P-glycoprotein): Yes means good, Lipophilicity: XLOGP3 value between −0.7 and +5.0 means good, Polarity: TPSA between 20 and 130 $Å^2$ means good, Water Solubility (Log S scale: Insoluble < -10 < Poorly < -6 < Moderately < -4 < Soluble < -2 < Very < 0 < Highly): Log S value not higher than 6 means good, Saturation (Fraction Csp3): Fraction of carbons in the sp3 hybridization not less than 0.25 means good, and Flexibility (Rotatable bonds): No more than 9 rotatable bonds means good

Table 3: Cytochrome P450 properties of phytocompounds

S.No.	PubChem (CID)	Compound Name	CYP1A2 inhibitor	CYP2C19 inhibitor	CYP2C9 inhibitor	CYP2D6 inhibitor	CYP3A4 inhibitor	Log K_p (Skin permeation) (cm/s)	A Bioavailability Score (ABS)
1.	8546	Pamoic acid	No	No	No	No	No	-4.56	0.56
2.	12305178	Fernenol	No	No	No	No	No	-2.51	0.55
3.	99474	Diosgenin	No	No	No	No	No	-4.80	0.55
4.	5281855	Ellagic acid	Yes	No	No	No	No	-7.36	0.55

5.	73170	Alpha-Amyrin	No	No	No	No	No	-2.51	0.55
6.	5280619	4,21-Dehydrogeissoschizine	No	No	No	No	No	-6.53	0.55
7.	5385014	Pleiocarpamine	No	No	No	Yes	No	-6.53	0.55
8.	293754	Amyrin acetate	No	No	No	No	No	-2.36	0.56
9.	107985	Triptolide	No	No	No	No	No	-8.34	0.55
10.	78358538	Vindolinine. 19-epimer, N-oxide.	No	No	No	Yes	No	-6.72	0.55
Synthetic drugs									
11.	31703	Adriamycin	No	No	No	No	No	-8.71	0.17

Note: No means good, the compound does not inhibit the CYP450 enzymes and does not give any adverse reactions; **Yes,** means the compound inhibits the CYP450 enzymes and gives unanticipated adverse reactions; The **more negative the log K_p,** the less skin permeant is the molecule; **ABS 0.55** means it passes the rule of five and **0.17** means it fails the rule of five.

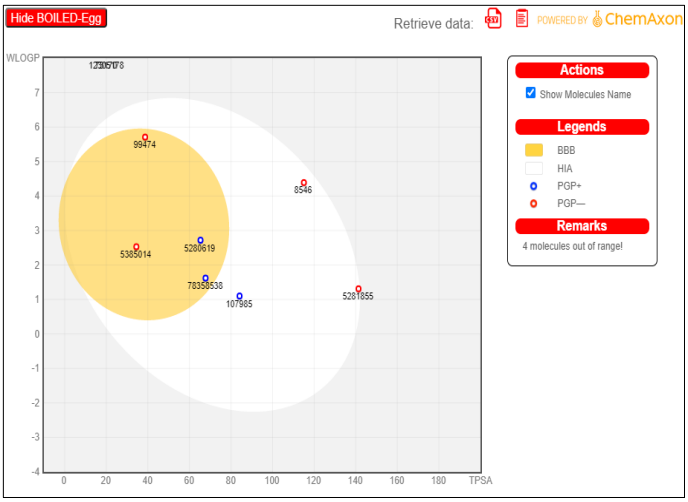

Figure 10: Boiled egg for all the compounds

Note: BBB: Points located in BOILED-Egg's yolk are molecules predicted to passively permeate through the blood-brain barrier. HIA- Points located in BOILED-Egg's white are molecules predicted to be passively absorbed by the gastrointestinal tract. PGP+: Blue dots are for molecules predicted to be effluated from the central nervous system by the P glycoprotein. PGP-: Red dots are for molecules predicted not to be effluated from the central nervous system by the P-glycoprotein.

DISCUSSION

Previous study reported that Grape seeds include polyphenolic and procyanidin chemicals, which have been demonstrated to reduce myeloperoxidase activity *in vitro* and *in vivo* tests. Grape seeds have been indicated as having the potential to prevent colon cancer cell development by changing the cell cycle, finally leading to caspase-dependent apoptosis [49]. A study reported that the phytocompound saponins was found in soybean. The extract of soybean had property to prevent the expression of protein kinase C and cyclooxygenase-2 which is responsible for the colon cancer [50].

Catechins from green tea improved apoptosis in colon cancer cells and decreased the expression of the vascular endothelial growth factor (VEGF) [27] and green tea leaves also inhibit the expression of matrix metalloproteinase 9 (MMP-9) [51]. Another study reported that the roots of garlic have allicin and organosulfur compounds increased cell death and prevented cancer cell growth by suppressing the expression of phosphoinositide 3-kinase [28].

In the same way, the present study reported that Pamoic acid from *Catharanthus roseus*, Fernenol from *Artemisia vulgaris*, and Diosgenin from *Solanum nigrum* has the potential ability to act as a drug for treating Colorectal Cancer.

CONCLUSION

In the present study, the phytocompounds from different Indian medicinal plants and the target protein Focal Adhesion Kinase (FAK) were subjected for *in silico* docking analysis to find the potential inhibitors for CRC. In which, 564 compounds showed better results than the Synthetic drug Adriamycin. Among them, 10 compounds showed very good binding affinity. Toxicity studies were done for the 10 best-interacted phytocompounds and the results showed that the compounds had very less toxicity. In which, the phytocompounds Pamoic acid, Fernenol, and Diosgenin showed the highest binding affinity among the other phytocompounds.

Hence, the present study concludes that the Pamoic acid from *Catharanthus roseus*, Fernenol from *Artemisia vulgaris*, and Diosgenin from *Solanum nigrum* may give a potential effect for treating CRC.

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Conflict of Interest

The authors declare that they have no conflict of interest.

ORCID ID

Dr. P. Ravikumar: https://orcid.org/0000-0002-2225-7785

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