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Identification of Anti-Cancer Lead Compounds from Crocus sativus: A Comprehensive Molecular Docking and QSAR Investigation

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ABSTRACT

Conventional cancer treatments like chemotherapy and radiotherapy are frequently bottlenecked by high toxicity, severe side effects, and astronomical development costs. Consequently, plant-derived bioactive secondary metabolites have emerged as promising, low-toxicity alternatives in modern drug discovery. Saffron (*Crocus sativus* L.) contains four major therapeutic carotenoids and monoterpene aldehydes: crocin, crocetin, picrocrocin, and safranal. This study evaluates their therapeutic efficacy against the tumor suppressor protein p53 using an integrated in silico approach pairing molecular docking with Quantitative Structure-Activity Relationship (QSAR) modelling. Molecular docking studies revealed that all four compounds localized within the vital DNA-binding domain of p53. Picrocrocin demonstrated the highest binding affinity (-6.01 kcal/mol), followed by safranal (-5.01 kcal/mol), crocetin (-4.43 kcal/mol), and crocin (-4.32 kcal/mol). Refined QSAR equations identified Topological Polar Surface Area (TPSA), octanol-water partition coefficient (LogP), and Molecular Refractivity (MR) as pivotal structural descriptors influencing biological activity. These computational findings provide a structural roadmap for prioritizing saffron-derived lead candidates, with safranal and picrocrocin standing out as optimal scaffolds for further preclinical optimization.

KEYWORDS: p53, saffron, bioactive metabolites, anti-cancerous, molecular docking, QSAR.

INTRODUCTION

The scientific exploration of bioactive metabolites present in plants is emerging as a competent resource in the competition for developing new drugs (Somasagara et al., 2012). Cancer is amongst the major health threats claiming millions of lives around the world on a regular basis (Jemal et al., 2009). In the present decade, the prevalence of cancer, its recurrence and severe side-effects of chemotherapeutic treatments brought about the resurgence of interests making the use of herbal preparations as more efficacious drugs with meager or no side-effects. Spices are dietetic food components ingested by most of the world population regularly to heighten the taste and flavour. (Premankur and Ramesh, 2010). The extracts of typically used condiments was shown to have high cytotoxicity on tumoral cell cultures (Unnikrishnan and Kuttan, 1988). Saffron, included amongst the most expensive spices, has been historically employed as a food colorant, cosmetic and drug in medicine (Amin and Buratovich, 2002; Samarghandhan and Borji,2014). The cultivation of saffron can be dated back to 2500-1500 BC and originated possibly in Iran, Greece and later became widespread in China, India, Eastern Europe and Mediterranean region (Tammaro, 1987). It is now cultivated diversely all over the world for its flavouring and medicinal perspectives.

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Volume1 |Issue1| July 2026
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Saffron spice is produced from the parched *Crocus sativus* L. stigmas, belonging to the Iridaceae family (Srivastava et al., 2010). In addition to riboflavin saffron possesses a rich source of carotenoids (Gutheil et al., 2012). *C sativus*is, a stem-less perennial herb (Rios et al., 1996), prefers infriable, loose, well-watered and well-drained calcareous soil. The plant is characterized by its narrow leaves and a corm which is a fleshy bulb (Kumar et al., 2009). According to chemical analyses four principle active ingredients isolated from saffron which composed of crocin, crocetin, picrocrocin and safranal Figure1. Crocin is a crocetingentiobiase ester and is water soluble. The major component of crocin, crocetin, is a diterpenic carotenoid (the aglycon of crocin) is 88′diapo-88′-carotenoic acid (Giaccio, 2009). Picrocrocin is a monoterpene glycoside (4-(β-D-glucopyranosyloxy)-2,6,6-trimethyl-1-cyclohexene-1-carboxyaldehyde). Picrocrocin is the chemical contributing to the bitter taste of saffron. Safranal, (2,6,6-trimethyl cyclohexa-1,3-dien-1-carboxyaldehyde) which is synthesized by the deglucosylation of picrocrocrocin (Schmidt et al., 2007; Zhang et al., 1994; Nair et al., 1995) constitutes the volatile agent of saffron whereas crocin and crocetin can be categorized as dyes responsible for colouring (Premankur and Ramesh, 2010). In addition to other carotenoids crocin, crocetin, picrocrocin and safranal are among of the most important saffron components to have anticancer and antitumor properties (Hosseini et al., 2018a; Yao et al., 2018). The method of operation of anti-cancerous and tumoricidal attributes of the engaging metabolites of saffron, crocin, crocetin, picrocrocin, and safranal are still unclear (Abdullaev and Frenkel, 1999). Crocetin, the major constituent of saffron, has sparked research curiosity owing to its multiple pharmaceutical impacts, including chemotherapeutic properties (Li et al., 2017). Additionally, reports claimed that carotenoids in saffron induce apoptosis, inhibit proliferation and synthesis of DNA, RNA, the supressive effect on free radical reactions, and proteins in various classes of cancer cells (Bathaie et al., 2013).It is an established fact that the cellular ratio of Bcl-2/Bax makes a cell either prone to cell proliferation or apoptosis, i.e., a higher Bcl-2/Bax ratio prevents a cell from undergoing apoptosis since Bcl-2 is part of the anti-apoptotic family whereas Bax is pro-apoptotic. Therefore, a lower Bcl-2/Bax ratio will induce cell death (Sarbia et al., 1997; Sedlak et al., 1995). Therefore, from literature survey, research indicates that crocetin, which is a key bioactive metabolite of saffron, increases cell permeability and induces cell death (Escribano et al., 1996). The remaining carotenoids have been reported to restrain DNA and protein synthesis (Abdullaev and Espinosa-Aguirre,2004). P53, commonly regarded as the "*guardian of the genome*" is a nuclear transcription factor. It is observed to have been mutated in every kind of cancer. p53 is also pro-apoptotic *i.e* in cells which have DNA damage or are undergoing stress, p53 is found to induce apoptosis (Sionoy and Haupt, 1999; Prives and Hall,1999; Vousden and Lu, 2002; Lacroix et al., 2006; El-Deiry,2003). In this study the therapeutic efficiency of the bioactive metabolites of saffron, crocin, crocetin, picrocrocin and safranal have been studied to discover whether these metabolites can induce p53-mediated apoptosis in cancer cells. Molecular docking is used to model interactions of the receptor which is generally a protein and a ligand which might be another protein or any small molecule such as a drug etc. and predicts the different ligand conformations on the catalytic site of the protein. The finest docked configuration can be chosen based on some docking scores generated by the tool being used such as ligand's binding energy, its efficiency and other parameters based on the acquired attributes of the tool being used (Meng et al., 2011). The docking tool uses different algorithms and most popularly used is Genetic Algorithm. Since, the bioactive components are probable anti-tumour agents therefore Quantitative Structure-Activity Relationship, QSAR, evaluation was executed to determine their chemical attributes along with varying biochemical functions such asLD_{50} and IC_{50}

values. To develop an association between the chemical properties of substances to their biological activities and to attain a reliable paradigm for prognostication of new chemical entities' activitieson which QSAR can be performed (Patel et al., 2014).

METHODOLOGY

Retrieval of frameworks of the bioactive metabolites

The carotenoids' three-dimensional frameworks namely crocin and crocetin, and the monoterpene aldehydes namely picrocrocin and safranal were retrieved from ChemSpider (Pence and William, 2010) with ChemSpider ID 4444645 for crocin, 4444644 for crocetin, 115678 for picrocrocin and 55000 for safranal. The structures from ChemSpider were in MOL format and were therefore transformed to PDB format using the offline variant of the software Open Babel; OpenBabel-2.4.0 (O'Boyle et al., 2011). The 3D organization visualization of the carotenoids was done with the aid of UCSF Chimera; Chimera 1.11.2 (Pettersen et al., 2004).

Physiochemical properties

The physicochemical attributes of the four metabolites of saffron had been retrieved from PubChem (Kim et al., 2016) in the form of melting point, molecular weight, molecular formula, number of hydrogen bond's donor and acceptor, number of rotatable bonds, TPSA, monoisotopic mass, XLogP3-AA, in addition to number of heavy atoms, numbers of stereocenter for defined atoms and defined bonds and covalently bonded atom count. The attributes mentioned were used for comparison among the compounds in terms of drug-likeness and structural diversity.

Molecular Binding Prediction: Molecular Docking

The structure of p53 protein was retrieved from Protein Data Bank (Protein ID- 1TUP) and preparation was accomplished by the standard steps required for docking. Ligand- receptor molecular binding inquiry was executed using offline AutoDockTools-1.5.6 (Morris et al., 1996) on windows platform. The employment of Auto Dock Tools was achieved with the available MGL tools. Docking of the four bioactive compounds crocin, crocetin, picrocrocin and safranal against p53 was completed with the aid of Lamarckian Genetic Algorithm. The p53 was kept as the macromolecule which has been kept as rigid and the ligands i.e. crocin, crocetin, picrocrocin and safranal were kept flexible. The grid was maintained in a specific manner so that the macromolecule and the ligands were submerged within the given grid parameters for the four individual ligands against the macromolecule.

Quantitative Structure Activity Relationship Investigation

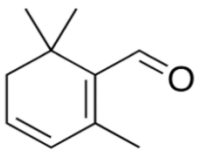
Quantitative structure Activity Relationship, QSAR was completed with a non-networked software tool Easy QSAR (Asthana et al., 2014). Crocin, crocetin, picrocrocin and safranal were analysed in relation to their molecular properties. The activity used for crocin, picrocrocin and safranal was Lethal Dose 50, LD_{50} (Abdullaev and Espinosa-Aguirre, 2004) whereas the activity used for crocin and crocetin was Inhibitory Concentration IC_{50} (Kim et al., 2016). The molecular features used as descriptors were created for the individual metabolites using Custom Computation in ChemDes (Jie et al., 2015). The molecular properties used as descriptors were Topological Polar Surface Area (TPSA), squared Moriguchioctanol-water partition coefficient ($logP_2$), hydrophilic factor (Hy), Unsaturation index (Ui), Morguchioctanol-water partition coefficient (logP), and molecular refractivity (MR). The input files provided for the generation of descriptor files were first and foremost transformed from mol format into smiles format.

RESULTS

Physiochemical properties

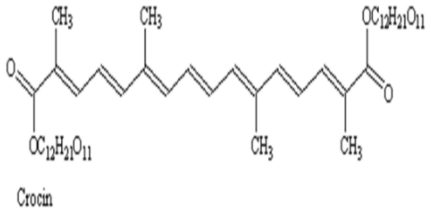
The physiochemical properties of the four bioactive metabolites are mentioned in the table, some of which were also salvaged fromChemSpider, apart from PubChem database (Table 1). The metabolites were found to exhibit discrepancy in polarity, molecular

size and flexibility with crocin representing the largest polar compound and safranal reportedly small and least polar.



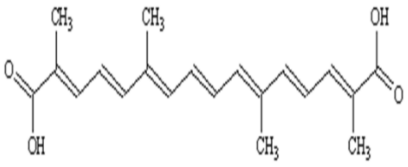
Safranal

(A)



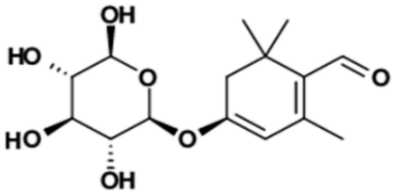
Crocin

(B)



Crocetin

(C)



Picrocrocin

(D)

Figure1: Showing the four bioactive compounds found in saffron namely: crocin, crocetin picrocrocin and safranal.

Molecular Docking Analyses

In this current study molecular docking of p53 with the four individual metabolites crocin, crocetin, picrocrocin, and safranal was performed employing AutoDock Tools and 10 docking conformations were developed for all the four metabolites. However, the conformer with the greatest bonding energy has been reported. The factors reported in Table 2 are ligand proficiency, bonding energy, inhibition constant, inter-molecular energy, vdw-hb-desolving energy, unbound energy, total intrinsic energy, rotational energy, clRMS, ref RMS. The maximum binding energy was noticed in picrocrocin with -6.01 followed by safranal with -5.01, crocetin with -4.43 and crocin with -4.32 respectively. The docking conformations which are represented in Figure 3, shows crocin, crocetin, picrocrocin, and safranal interacting with the DNA-binding junction of the p53 molecule. This observation could be accounted for, because the active metabolites of saffron inhibit cancer growth and proliferation by inhibiting DNA and RNA synthesis. Therefore, from the binding energies of all the four bioactive metabolites, picrocrocin shows maximum binding affinity with the most favourable predicted binding affinity and was tailed by safranal, crocetin and crocin. The graph of binding energy versus conformations had been generated for the total four bioactive metabolites and is represented via Figure 2. Mostly the interactions between p53 and the carotenoids revealed Vander Waals interactivity and few alkyl residues in addition to hydrogen bonded interactions. The amino acid interaction of p53 and the carotenoids are presented in Table 3, with picrocrocin showing

Volume1 |Issue1| July 2026
ISSN: PP: 49-60

interactions with Gln A:167, Ala B:276, Cys B:277, Ser B:121, Thr B: 123, and Gln B136**.**

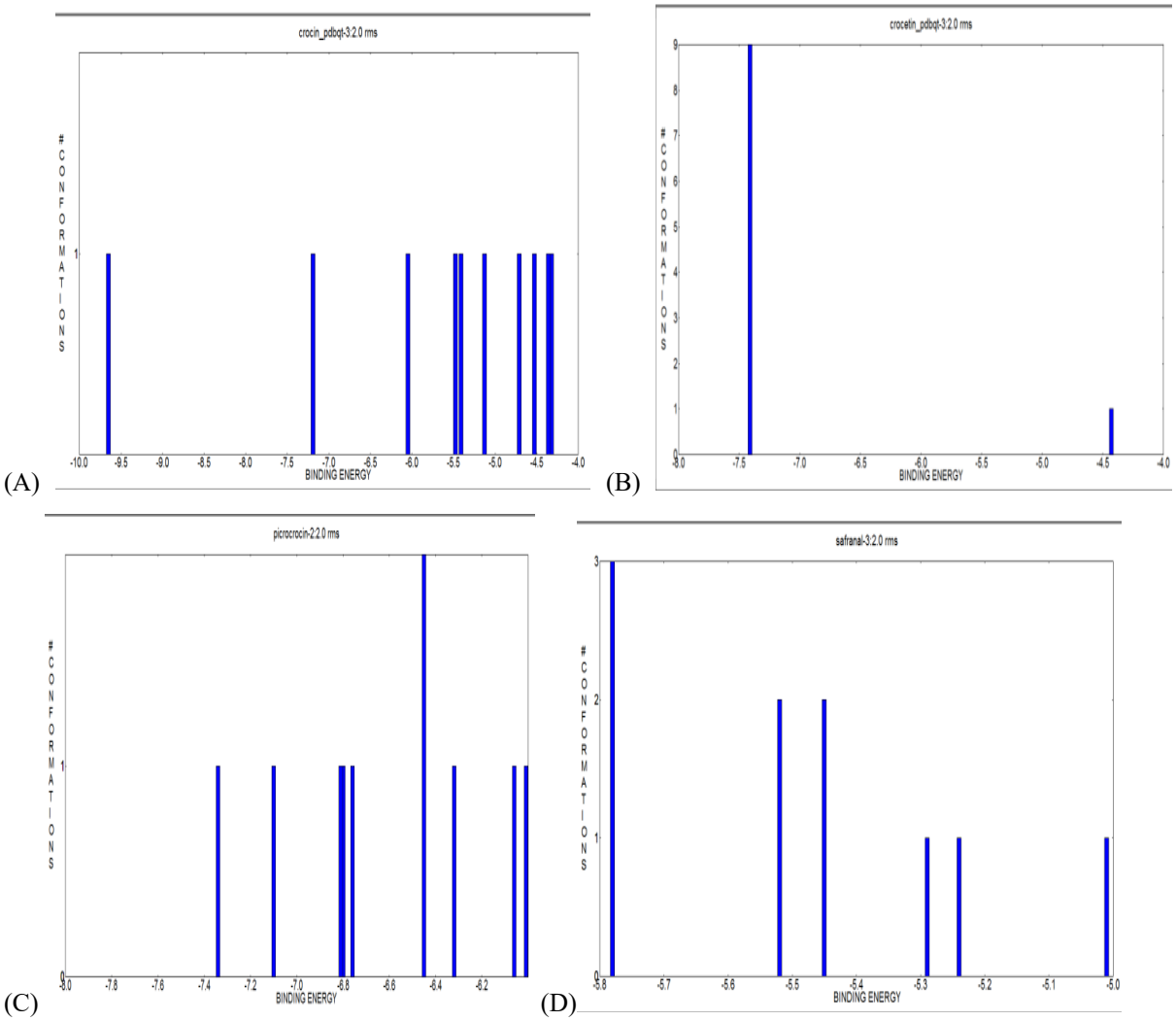


Figure 2: The graph of binding energy vs. conformations (2.0 clustering) of (A) crocin, (B) crocetin, (C) picrocrocin, (D) safranal. This was generated by the integrated commands in AutoDock tools after the conformations were formed. Out of 10 conformations, the best pose was selected based on their binding energies.

Volume1 |Issue1| July 2026
ISSN: PP: 49-60

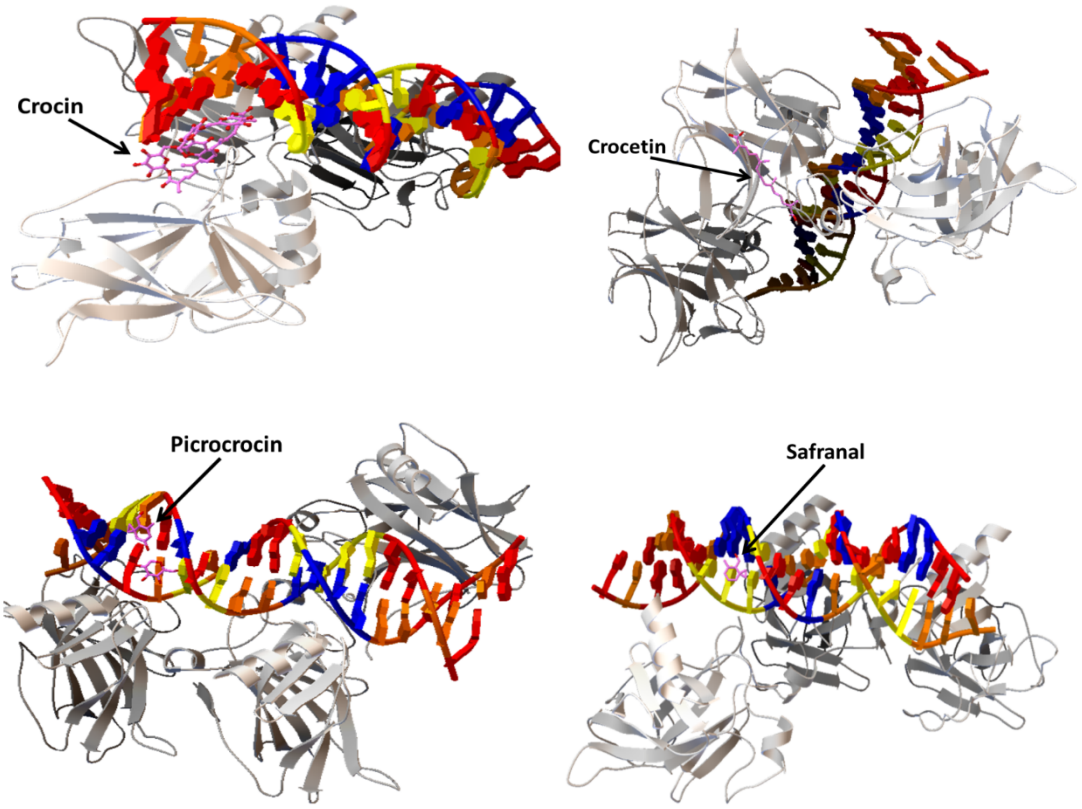


Figure3: Docking results of the four bioactive metabolites of saffron, crocin, crocetin, picrocrocin, safranal with p53 as generated using AutoDockTools-1.5.6.Lamarkian Genetic algorithm was chosen while carrying out the molecular docking sessions between the rigid macromolecule (p53) and the flexible ligands (i.e crocin, crocetin, picrocrocin and safranal respectively).

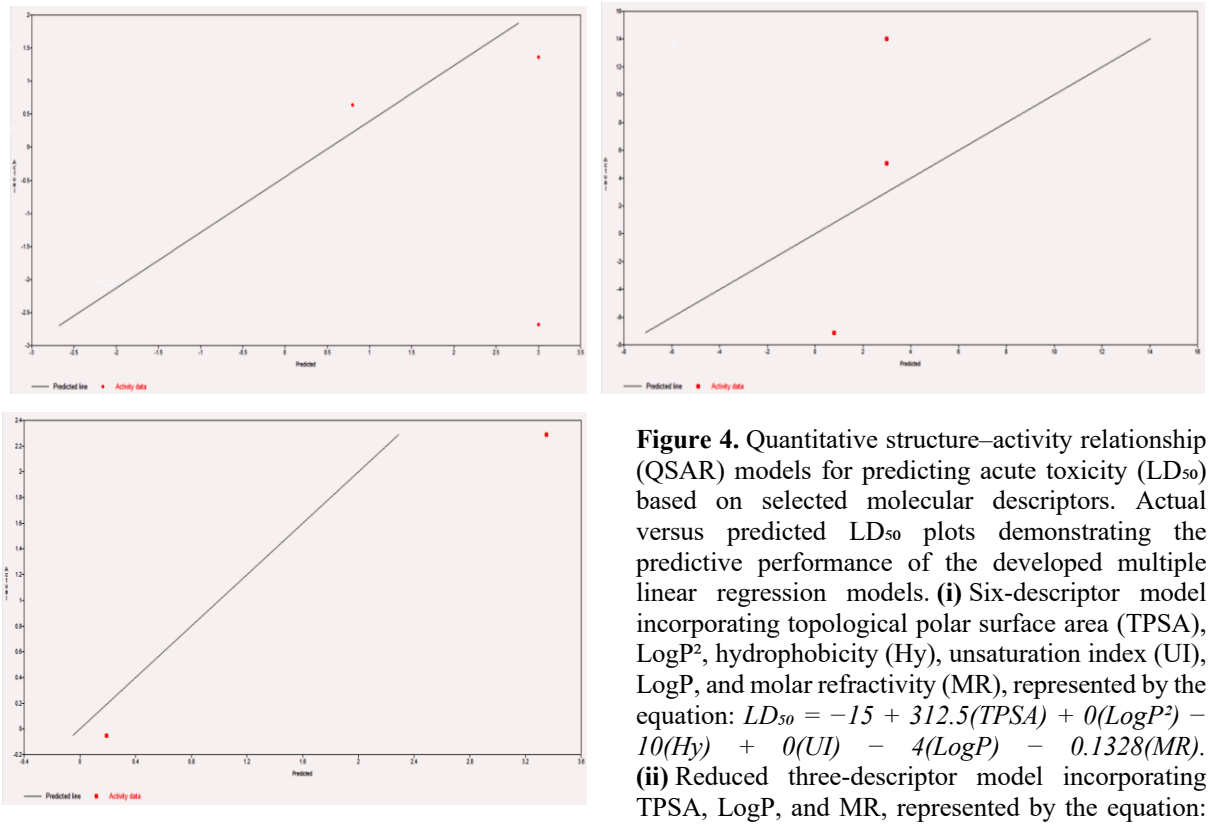


Figure 4. Quantitative structure–activity relationship (QSAR) models for predicting acute toxicity (LD_{50}) based on selected molecular descriptors. Actual versus predicted LD_{50} plots demonstrating the predictive performance of the developed multiple linear regression models. **(i)** Six-descriptor model incorporating topological polar surface area (TPSA), $LogP^2$, hydrophobicity (Hy), unsaturation index (UI), LogP, and molar refractivity (MR), represented by the equation: $LD_{50} = -15 + 312.5(TPSA) + 0(LogP^2) - 10(Hy) + 0(UI) - 4(LogP) - 0.1328(MR)$. **(ii)** Reduced three-descriptor model incorporating TPSA, LogP, and MR, represented by the equation: $LD_{50} = 5.5313 - 0.0195(TPSA) - 1.2500(LogP) - 0.0313(MR)$.

Table 1**:** The chemical and physical properties of crocin, crocetin, picrocrocin have been summarized in the table.

Sl. No.	**Parameters**	**Bioactive compounds**			
		Crocin	**Crocetin**	**Picrocrocin**	**Safranal**
1	PubChem CID	5281233	5281232	130796	61041
2	Molecular Formula	$C_{44}H_{64}O_{24}$	$C_{20}H_{24}O_4$	$C_{16}H_{26}O_7$	$C_{10}H_{14}O$
3	Molecular Weight (g/mol)	976.972	328.408	330.377	150.221
4	Melting Point	185˚C	285˚C *	209.65˚C *	< 25˚C
5	Hydrogen Bond Donor Count	14	2	4	0
6	Hydrogen Bond Acceptor Count	24	4	7	1
7	Rotatable Bond Count	20	8	4	1
8	TPSA	391 A^2	74.6 A^2	116 A^2	17.1 A^2
9	Monoisotropic mass (g/mol)	976.3799	328.167	330.168	150.104
10	XLogP3-AA	-2.5	5.4	-0.5	2.1
11	Heavy atom count	68	24	23	11
12	Defined Atom Stereocenter Count	20	0	6	0
13	Defined Bond Stereocenter Count	7	7	0	0
14	Covalently Bonded Unit Count	1	1	1	1

* The melting points of crocetin and picrocin have been retrieved from ChemSpider.

Table 2**:** The different parameters generated because of docking p53 with the different ligands (crocin, crocetin, picrocrocin, safranal) have been computed and listed above. The values were computed with Auto Dock tools while generating the conformations along with their binding energies and other computation values.

Receptor	1TUP			
Ligand	**Crocin**	**Crocetin**	**Picrocrocin**	**Safranal**
Binding energy	-4.32	-4.43	-6.01	-5.01
Ligand efficiency	-0.06	-0.18	-0.26	-0.46
Inhibition constant (μmol)	686.82	570.48	39.45	211.05
Intermolar energy	-9.68	-7.41	-7.2	-5.01
vdw-hb-desolving energy	-0.96	-6.75	-7.12	-4.96
Electrostatic Energy	-0.06	-0.66	-0.08	-0.05
Total internal energy	-7.95	-0.71	-0.28	0
Torsional energy	5.37	2.98	1.19	0
Unbound energy	-7.95	-0.71	-0.28	0
clRMS	0	0	0	0
refRMS	24.33	34.03	35.66	31.77

Table 3**:** Showing the amino acids interacting with the p53 (1TUP) molecule, along with their position, chain and the type of interactions.

Receptor	Ligand	Amino acid position	Type of interaction
1TUP	Crocin	Lys C: 120, Glu C: 198, Thr B: 211, Ser B: 96, Glu B: 171	Unfavourable donor-donor interactions
		Asn B: 210, Gly C: 199	Conventional hydrogen bond
		His B, 168, Lys C: 139	Alkyl
		Cys C: 277, Asn C: 235, Ser C: 121, Thr C: 123, Arg B: 249, Gln B: 167, Thr C: 140, Val B: 97, Leu C: 201, Thr B: 170, Phe B: 212, Arg B: 213, Val B: 172, Arg C: 196	Van der Waals
	Crocetin	Arg B: 248	Hydrogen bond
	Picrocrocin	Gln A: 167, Ala B: 276, Cys B: 277, Ser B: 121, Thr B: 123, Gln B: 136	Van der Waals
		Ser A: 166	Unfavourable donor-donor bond
		Lys B: 139	Alkyl
	Safranal	Ser A: 166, Gln A: 165, Gln A: 167, Gln B: 136, Ser B: 121, Lys B: 120	Van der Waals
		Ala B: 276, Cys B: 277	Alkyl

Quantitative Structure Activity Relationship Analyses

Since crocin, crocetin, picrocrocin, safranal can be potential drug candidates therefore Quantitative Structure-Activity Relationship, QSAR was carried out to anticipate their biological action with the chemical structures. Crocin, picrocrocin and safranal were analysed in relation to their molecular properties i.e the descriptor file contained molecular properties as generated from ChemDes and the activity chosen was LD_{50}. After performing QSAR studies a statistical analysis was initiated from which the F statistics calculated was 0.733 with a critical F of 19.33. The percentage contribution of each descriptor to activity was 49.75% of TPSA, 9.48% of LogP2, 25.19% of Hy, 8.33% of UI, 63% of LogP, and 41.68% of MR. Also, the correlation of descriptors with activity generated was 0.71 for TPSA, 0.31 for LogP2,-0.50 for Hy, 0.29 for UI, -0.79 for LogP, and 0.65 for MR. A plot was generated of actual vs. predicted activity with the QSAR equation Figure 4 (i). The actual values were 3mM, 3mM, and 0.8mM for crocin, picrocrocin and safranal respectively and the predicted values were 14.02, 5.06 and -7.12. Since for a better prediction the percentage contribution of descriptor to activity is around 50% and for a good correlation the threshold chosen was around 0.7 therefore the analysis was re-executed by taking only TPSA, LogP and MR as descriptors. A plot was generated for the real versus expected activity with the generated QSAR equation Figure 4 (ii). The F statistics calculated was 0.28 and the critical F value was 19.16. The predicted values were -2.69, 1.36 and 0.64. Using IC_{50} values of crocin and crocetin QSAR studies was again carried out to summarize their activity with their chemical structure. The F statistics calculated was 0.32 and the critical F value was 233.39. The percentage contribution of each descriptor to activity and correlation of descriptors with activity was not reported. This could have been an outcome resulting from fewer number of parameters chosen for the study. The actual IC_{50} values were 3.35 mmol/l and 0.19 mmol/l, and the predicted values calculated were 2.29 and -0.05 for crocin and crocetin respectively. A plot

was generated for actual vs. predicted activity along with the QSAR equation Figure 5 (iii).

DISCUSSIONS

The survey on the naturopathic treatment using saffron to obviate and in curing of cancer was rooted on the extract from the parched *Crocus sativus* stigmas having anti-cancerous properties (Srivastava et al., 2010; Zhang et al., 1994). This study explored the anticancer potential of saffron metabolites through docking and QSAR analysis. The four active carotenoid secondary metabolites of saffron viz. crocin, crocetin, safranal and picrocrocin reportedly possess diverse pharmacological impacts including cytoprotective, antioxidant as well as antitumor effects via inhibition of cell growth, apoptosis, etc. (Abdullaev and Frenkel,1999; Amin and Buratovich, 2007). p53 typically regarded as the "*guardian of the genome*" is a gene regulating cellular stress and genetic damage and is found to have oncogenic potential when mutated. p53 is found to induce its pro-apoptotic functions in response to cellular insults such as DNA damage (Sionoy and Haupt, 1999; Vousden and Lu, 2009). It is well documented that all the four bioactive metabolites of saffron can suppress the proliferation of cancer cells both *in-vitro* and *in-vivo*. Crocetin has been evidenced to hamper the multiplication of tumor cells by enhancing the proportion of Bax/Bcl-2, which in turn induces apoptosis and ultimately tumour formation (Sarbia et al,.1997; Sedlak et al., 1995). From the studies, the discrepancy of the predicted LD_{50} from actual LD_{50} value was the least insafranal followed by the actual and predicted IC_{50} value of crocetin, crocin and LD_{50} value of picrocrocin and crocin. Therefore, safranal can be further tested for potential anti-cancer and anti-tumor drug candidate.

Despite saffron and its components possessing many therapeutic effects they do also posses stheir fair share of limitations. Safranal, though show several pharmacological effects such as inflammation and antioxidant activity, it is an aromatic substance and therefore represent a major volatile component of saffron (Esmaealzadehet al., 2023). Crocin had been studied extensively and was found to exhibit pharmacological effects as a cardioprotectant and neuroprotectant and is also water soluble, but has poor oral absorptivity (Song et al., 2021). In the intestine crocin is broken down into crocetin and this substance can reach CNS by penetrating blood-brain barrier transcellular diffusion hence is effective in neurodegeneration, but its plasma concentration level is low (Hosseini et al., 2018b). Additionally, since very limited numbers of compounds were used for QSAR analysis there is a constrained factor in the model stability. With few data points the model statistics can be unstable, and a single deviant can distort the apparent relationship between structure and activity.

Regardless, the study presents a relevant and worthwhile preliminary computational investigation into the anticancer potential of saffron-derived metabolites and further analysis can be carried out such as checking which metabolite is acting against which form of cancer and how much is their potential to curb the disease. Additionally, the compounds can be considered promising leads as therapeutic candidates and could be explored more in this direction. Picrocrocin is relatively less studied and its binding affinity with p53 being the highest in this study has open a way for more exploration on this compound.

CONCLUSIONS

The present study accentuates the promising anti-cancer quality of saffron's bioactive compounds specifically crocetin, crocin, picrocrocin and safranal, by means of physicochemical properties, molecular docking simulations and QSAR analyses. Pubchem and Chemspider obtained data inveterate effective drug-like properties supported by molecular docking analyses with binding energies of -6.01 kcal/mol (picrocrocin), -5.01 kcal/mol (safranal), -4.43 kcal/mol (crocetin), and -4.32 kcal/mol (crocin), predominantly driven through van der Waals, alkyl, and interactions between hydrogen bridge with key residues (Table 3). These binding energies suggest

effective inhibition and blockage of DNA and RNA synthesis mechanisms successfully curbing cancer cells proliferation and induce apoptosis. Refined key descriptors such as TPSA, LogP, and MR in QSAR analyses yielded F-statistics up to 0.733 and correlations ≥0.65 further validating structure activity correlations between the actual and predicted values, underscoring their structural stability as drug candidates. To summarize, saffron's metabolites have promising potential as tumor suppressants with safranal as the most viable candidate warranting further preclinical validation because of its superior predictive binding accuracy. Further research could be done by evaluating combinations with other chemotherapeutics or natural products to increase these metabolites' effectiveness.

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CONFLICT OF INTEREST

The author declares no conflict of interest.

REFERENCES

Abdullaev, F. I., & Espinosa-Aguirre, J. J. (2004). Biomedical properties of saffron and its potential use in cancer therapy and chemoprevention trials. *Cancer Detection and Prevention, 28*(6), 426–432.https://doi.org/10.1016/j.cdp.2004.09.002

Abdullaev, J. F., & Frenkel, G. D. (1999). Saffron in biological and medical research. In M. Negbi (Ed.), *Saffron: Crocus sativus L.* (pp. 103–113). Harwood Academic Publishers.

Amin, A., & Buratovich, M. (2007). The anti-cancer charm of flavonoids: A cup-of-tea will do! *Recent Patents on Anti-Cancer Drug Discovery, 2*(2), 109–117.https://doi.org/10.2174/157489207780832414

Asthana, S., Agarwal, T., Khursheed, A., & Dutta, D. (2014). Molecular modeling and QSAR analysis to explore therapeutic potentials of phytoestrogens in osteoporosis. *International Journal of Pharmacy and Pharmaceutical Sciences, 6*(3), 239–243.

Bathaie, S. Z., Hoshyar, R., Miri, H., & Sadeghizadeh, M. (2013). Anticancer effects of crocetin in both human adenocarcinoma gastric cancer cells and rat model of gastric cancer. *Biochemistry and Cell Biology, 91*(6), 397–402.https://doi.org/10.1139/bcb-2013-0014

El-Deiry, W. S. (2003). The role of p53 in chemosensitivity and radiosensitivity. *Oncogene, 22*(47),7486–7495. https://doi.org/10.1038/sj.onc.1206949

Escribano, J., Alonso, G. L., Coca-Prados, M., & Fernández, J. A. (1996). Crocin, safranal and picrocrocin from saffron (*Crocus sativus* L.) inhibit the growth of human cancer cells in vitro. *Cancer Letters, 100*(1–2), 23–30. https://doi.org/10.1016/0304-3835(95)04067-6

Esmaealzadeh, D., Moodi Ghalibaf, A., Shariati Rad, M., Rezaee, R., Razavi, B. M., & Hosseinzadeh, H. (2023). Pharmacological effects of safranal: An updated review. *Iranian Journal of Basic Medical Sciences, 26*(10), 1131–1143. https://doi.org/10.22038/IJBMS.2023.69824.15197

Giaccio, M. (2004). Crocetin from saffron: An active component of an ancient spice. *Critical Reviews in Food Science and Nutrition, 44*(3), 155–172. https://doi.org/10.1080/10408690490441433

Gutheil, W. G., Reed, G., Ray, A., Anant, S., & Dhar, A. (2012). Crocetin: An agent derived from saffron for prevention and therapy for cancer. *Current Pharmaceutical Biotechnology, 13*(1), 173–179. https://doi.org/10.2174/138920112798868566

Hosseini, A., Razavi, B. M., & Hosseinzadeh, H. (2018). Pharmacokinetic properties of saffron and its active components. *European Journal of Drug Metabolism and Pharmacokinetics, 43*(4), 383–390. https://doi.org/10.1007/s13318-017-0449-3

Hosseini, A., Razavi, B. M., & Hosseinzadeh, H. (2018). Saffron (*Crocus sativus*) petal as a new pharmacological target: A review. *Iranian Journal of Basic Medical Sciences, 21*(11), 1091–1099. https://doi.org/10.22038/ijbms.2018.31243.7529

Jemal, A., Siegel, R., Ward, E., Hao, Y., Xu, J., & Thun, M. J. (2009). Cancer statistics. *CA: A Cancer Journal for Clinicians, 59*(4), 225–249. https://doi.org/10.3322/caac.20006

Jia, D., Dong-Sheng, C., Hong-Yu, M., Shao, L., Bai-Chuan, D., Yong-Huan, Y., Ning-Ning, W., Ai-

Ping, L., Wen-Bin, Z., & Alex, C. (2015). ChemDes: An integrated web-based platform for molecular descriptor and fingerprint computation. *Journal of Cheminformatics, 7*, 60. https://doi.org/10.1186/s13321-015-0109-z

Kim, S., Thiessen, P. A., Bolton, E. E., Chen, J., Fu, G., Gindulyte, A., Han, L., He, J., He, S., Shoemaker, B. A., Wang, J., Yu, B., Zhang, J., & Bryant, S. H. (2016). PubChem: Substance and compound databases. *Nucleic Acids Research, 44*(D1), D1202–D1213. https://doi.org/10.1093/nar/gkae1059

Kumar, R., Singh, V., Devi, K., Sharma, M., Singh, M. K., & Ahuja, P. S. (2009). State of art of saffron (*Crocus sativus* L.) agronomy: A comprehensive review. *Food Reviews International, 25*(1), 44–85. https://doi.org/10.1080/87559120802458503

Lacroix, M., Toillon, R.-A., & Leclercq, G. (2006). p53 and breast cancer, an update. *Endocrine-Related Cancer, 13*(2), 293–325. https://doi.org/10.1677/erc.1.01172

Li, S., Shen, X. Y., Ouyang, T., Qu, Y., Luo, T., & Wang, H. Q. (2017). Synergistic anticancer effect of combined crocetin and cisplatin on KYS cells via p53/p21 pathway. *Cancer Cell International, 17*, 98. https://doi.org/10.1186/s12935-017-0468-9

Meng, X. Y., Zhang, H. X., Mezei, M., & Cui, M. (2011). Molecular docking: A powerful approach for structure-based drug discovery. *Current Computer-Aided Drug Design, 7*(2), 146–157. https://doi.org/10.2174/157340911795677602

Morris, G. M., Goodsell, D. S., Huey, R., & Olson, A. J. (1996). Distributed automated docking of flexible ligands to proteins: Parallel applications of AutoDock 2.4. *Journal of Computer-Aided Molecular Design, 10*, 293–304. https://doi.org/10.1007/BF00124499

Nair, S. C., Kurumboor, S. K., & Hasegawa, J. H. (1995). Saffron chemoprevention in biology and medicine: A review. *Cancer Biotherapy, 10*(4), 257–264.https://doi.org/10.1089/cbr.1995.10.257

O'Boyle, N. M., Banck, M., James, C. A., Morley, C., Vandermeersch, T., & Hutchison, G. R. (2011). Open Babel: An open chemical toolbox. *Journal of Cheminformatics, 3*, 33. https://doi.org/10.1186/1758-2946-3-33

Patel, H. M., Noolvi, M. N., Sharma, P., Jaiswal, V., Bansal, S., Lohan, S., Kumar, S. S., Abbot, V., Dhiman, S., & Bhardwaj, V. (2014). Quantitative structure-activity relationship studies as strategic approach in drug discovery. *Medicinal Chemistry Research, 23*(12), 4991–5007. https://doi.org/10.1007/s00044-014-1072-3

Pence, H. E., & Williams, A. (2010). ChemSpider: An online chemical information resource. *Journal of Chemical Education, 87*(11), 1123–1124. https://doi.org/10.1021/ed100697w

Pettersen, E. F., Goddard, T. D., Huang, C. C., Couch, G. S., Greenblatt, D. M., Meng, E. C., & Ferrin, T. E. (2004). UCSF Chimera—A visualization system for exploratory research and analysis. *Journal of Computational Chemistry, 25*(13), 1605–1612. https://doi.org/10.1002/jcc.20084

Premkumar, K., & Ramesh, A. (2010). Anticancer, anti-mutagenic and antioxidant potential of saffron: An overview of current awareness and future perspectives. *Functional Plant Science and Biotechnology*, Special Issue 2, 91–97. https://www.researchgate.net/profile/Amjad-Husaini/publication/283796680_Saffron/links/5647c35b08ae9f9c13e9600d/Saffron.pdf#page=100

Prives, C., & Hall, P. A. (1999). The p53 pathway. *The Journal of Pathology, 187*(1), 112–126.https://doi.org/10.1002/(SICI)10969896(199901)187:1<112::AID-PATH250>3.0.CO;2-3

Ríos, J. L., Recio, M. C., Giner, R. M., & Máñez, S. (1996). An update review of saffron and its active constituents. *Phytotherapy Research, 10*(3), 189–193.https://doi.org/10.1002/(SICI)1099-1573(199605)10:3<189::AID-PTR754>3.0.CO;2-C

Samarghandian, S., & Borji, A. (2014). Anticarcinogenic effect of saffron (*Crocus sativus* L.) and its ingredients. *Pharmacognosy Research, 6*(2), 99–107. https://doi.org/10.4103/0974-8490.128963

Sarbia, M., Bittinger, F., Grabellus, F., Verreet, P., Dutkowski, P., Willers, R., & Gabbert, H. E. (1997). Expression of Bax, a pro-apoptotic member of the Bcl-2 family, in esophageal squamous cell carcinoma. *International Journal of Cancer, 73*(4), 508–513.https://doi.org/10.1002/(sici)1097-0215(19971114)73:4<508::aid-ijc9>3.0.co;2-3

Schmidt, M., Betti, G., & Hensel, A. (2007). Saffron in phytotherapy: Pharmacology and clinical uses. *Wiener Medizinische Wochenschrift, 157*(13–14), 315–319. https://doi.org/10.1007/s10354-007-0428-4

Sedlak, T. W., Oltvai, Z. N., Yang, E., Wang, K., Boise, L. H., Thompson, C. B., & Korsmeyer, S. J. (1995). Multiple Bcl-2 family members demonstrate

Volume1 |Issue1| July 2026
ISSN: PP: 49-60

selective dimerization's with Bax. *Proceedings of the National Academy of Sciences, 92*(17), 7834–7838.https://doi.org/10.1073/pnas.92.17.7834

Sionov, R. V., & Haupt, Y. (1999). The cellular response to p53: The decision between life and death. *Oncogene, 18*(45), 6145–6157. https://doi.org/10.1038/sj.onc.1203130

Somasagara, R. R., Hegde, M., Chiruvella, K. K., Musini, A., Choudhary, B., & Raghavan, S. C. (2012). Extracts of strawberry fruits induce intrinsic pathway of apoptosis in breast cancer cells and inhibits tumor progression in mice. *PLoS ONE, 7*(10), e47021. https://doi.org/10.1371/journal.pone.0047021

Song, Y. N., Wang, Y., Zheng, Y. H., Liu, T. L., & Zhang, C. (2021). Crocins: A comprehensive review of structural characteristics, pharmacokinetics and therapeutic effects. *Fitoterapia, 153*, 104969. https://doi.org/10.1016/j.fitote.2021.104969

Srivastava, R., Ahmed, H., Dixit, R. K., Dharamveer, & Saraf, S. A. (2010). *Crocus sativus* L.: A comprehensive review. *Pharmacognosy Reviews, 4*(8), 200–208. https://doi.org/10.4103/0973-7847.70919

Tammaro, F. (1990). *Crocus sativus* L.—cv. Piano di Navelli (L'Aquila saffron): Environment, cultivation, morphometric characteristics, active principle, uses. In F. Tammaro & L. Marra (Eds.), *Proceedings of the International Conference on Saffron* (*Crocus sativus* L.) (pp. 47–57).

Unnikrishnan, M. C., & Kuttan, R. (1988). Cytotoxicity of extracts of spices to cultured cells. *Nutrition and Cancer, 11*(4), 251–256. https://doi.org/10.1080/01635588809513995

Vousden, K. H., & Lu, X. (2002). Live or let die: The cell's response to p53. *Nature Reviews Cancer, 2*(8), 594–604. https://doi.org/10.1038/nrc864

Yao, C., Liu, B. B., Qian, X. D., Li, L. Q., Cao, H. B., Guo, Q. S., & Zhou, G. F. (2018). Crocin induces autophagic apoptosis in hepatocellular carcinoma by inhibiting Akt/mTOR activity. *OncoTargets and Therapy, 11*, 2017–2028. https://doi.org/10.2147/OTT.S154586

Zhang, Y., Shoyama, Y., Sugiura, M., & Saito, H. (1994). Effects of *Crocus sativus* L. on the ethanol-induced impairment of passive avoidance performances in mice. *Biological and Pharmaceutical Bulletin, 17*(2), 217–221. https://doi.org/10.1248/bpb.17.217