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A Review on Triadax Pro cumbens as a anti cancer drug

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ABSTRACT-
A very promising species, Tridax procumbens, is known to produce secondary metabolites with a range of purported medical benefits, including anaesthetic, anti-inflammatory, anti- diabetic, and anti-anemic activities.Different communities have used this species in traditional ways for a very long time. The structural characteristics of luteolin have been studied computationally. A simulated screening of the characteristics of ADMET has anticipated the molecule's drug-likeness. The in-silico method uses the molecular docking technique to examine the development of complexes between proteins and ligands. Molecular dynamics (MD) simulations are used to examine the molecule's stability and reactivity. In the current study, we have made an effort to solidify the potential of any phytochemical from Tridax Procumbens as an inhibitor of human lung cancer.
Keywords: Molecular Docking, Molecular Dynamics Simulations, MCM7, DFT analysis

I. INTRODUCTION.-

Malignant growth is one of the destructive illnesses present in our reality that significantly grants in the worldwide passing proportion, yet it is serious. It tends to be characterized as the course of nusual and uncontrolled cell division that happens inside the human body and attack different parts, obliterating body tissues [1]. It can influence any organ like the lung, kidney, digestive system, uterus, mind, and even blood [2]. World Health Organization (WHO) has announced 9.6 million passings, or one out of six passings, in 2018 and expressed that disease is the subsequent driving reason for death overall [3]. The Globocan report 2020 gave by WHO announced that cellular breakdown in the lungs is the subsequent sickness bestowing 11.4% of the complete disease cases after bosom malignant growth (11.7%) [4]. Cellular breakdown in the lungs has the most noteworthy death pace of 2.21 million instances of the complete passings recorded from malignant growth in 2020 [4]. The dysregulation of deoxyribose nucleic corrosive (DNA) is the significant justification behind malignant growth commencement and movement in the human body [5]. Minichromosome upkeep (MCM) complex is the fifth most normal kind of disease that prompts the advancement of he pre-replication process for DNA [6]. The guideline of MCM protein in the human body prompts the expansion of different kinds of tumors [7]. MCM7 assumes an imperative part in malignant growth improvement and movement and goes about as an initiator in eukaryotic DNA and G1/S cell cycle proliferation [8]. It is one among the group of MCM DNA helicase including six monitored proteins called MCM2-7 [9]. It was first separated from Saccharomyces cerevisiae (sprouting yeast) [10]. This cycle is called DNA replication permitting in which the MCM complex loosens up the limited strands of the DNA [11]. This loosening up prompts genome duplication in multiplying cells and chromosomal deformities. Such chromosomal deformities result in tumorigenesis [12]. MCM proteins are viewed as exceptionally engaged with human disease development and harmful changes.

Hence, the MCM proteins are viewed as promising focuses for malignant growth drug advancement. Then again, over the most recent couple of many years, restorative spices have been moved from periphery to standard use, and a more number of individuals look for cures in home grown extricates [13, 14]. Plants have forever been a significant wellspring of against harmful enhancements. Regular concentrates share an enormous part in anticancer medications accessible in the business sectors. Many examinations have been accounted for against malignant growth infirmities from home grown separates like gedunin for ovarian disease [15], ginsenoside for bosom disease [16], cinnamon [17], and some more. These discoveries have persuaded us to work explicitly on home grown separates. For the current work, we have considered a tropical plant Tridax

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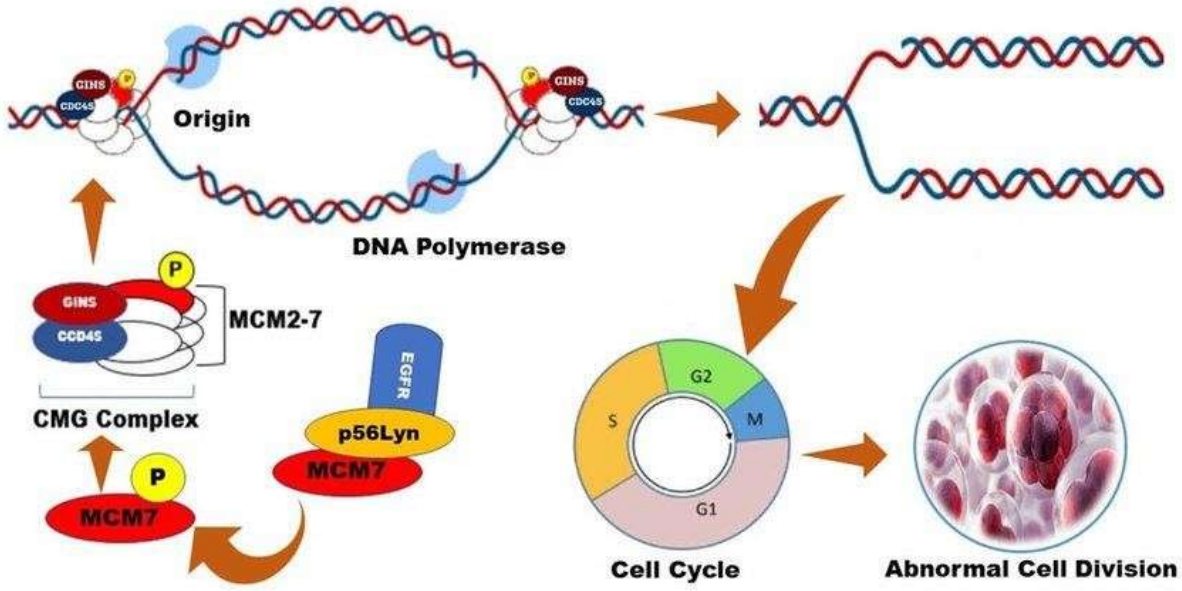
procumbens. This plant has verifiable smidgens of proof for being utilized as a therapeutic plant [18]. The plant is local to Asia, America, Africa and, Australia. In numerous nations, Tridax procumbens is broadly utilized for the mending of serious injuries [18]. This spice is additionally known for its great many pharmacological exercises like enemy of contagious [19], calming [20], against tubercular [21], hepatoprotective [22], hostile to diabetic [23] and so on. It is additionally known for relieving asthma [24] and is a satisfied spice with optional metabolites like steroids, terpenoids, tannins, flavonoids, saponins, glycosides, and amino acids [25].

The virtual screening of pharmacological properties is finished for Luteolin to concentrate on its medication like similarities. The energy improvement of the construction of Luteolin is finished to research its solidness. The limiting of ligand to protein is accounted by performing sub-atomic docking, and the security of the complex shaped by docking of protein and ligand is checked by playing out the atomic elements recreations. In the current paper, an in silico study finished with luteolin as an inhibitor will help in laying out areas of strength for the of luteolin as a possible medication against human disease.

II. MATERIAL AND METHODS.-

Potential target protein structure for cancer MCM7 protease

Human malignant growth encodes countless protein structures. The construction we have considered for this study is protease MCM7 (PDB ID: 6XTX, goal: 3.29 Å). MCM7 can metastasize and obliterate the living tissues in the body. The malignancies wherein MCM7 is involved are hepatocellular carcinoma, head, and neck, throat, and so on [26]. Hence, reasonable to plan a review will distinguish the compound with inhibitor action for forestalling replication of DNA of destructive cells. The 3D design of protein MCM7 is downloaded from "Protein Data Bank."



Expected inhibitor: Tridax procumbens

Tridax procumbens is a phytochemical-rich plant comprising baicalin, tetrandrine, luteolin, apigenin, stigmasterol, catechin, epicatechin, quercetin, myricetin, gallocatechin, sitosterol, akuammidine, kaempferol, and a lot more [27]. Among every one of the phytochemicals, luteolin is a flavonoid having hostile to malignant properties [28]. Various works have been done as such far detailing the anticancer properties of Luteolin [29]. Anticancer movement of luteolin is examined against gastric diseases [30], bosom malignant growth [31], prostate disease [32], cerebrum cancers [33], cervical malignant growth [34], skin malignant growth [35], and so on. Along these lines, it ensures that our vision to involve it as an

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enemy of disease specialist won't frustrate us. Luteolin is a flavonoid having a place with the vitamin B family. It is chiefly present in numerous food supplements like parsley, broccoli, onion leaves, carrots, peppers, cabbages, apple skins, and so on [36]. It is exceptionally added as a food supplement because of its enemy of oxidative property. Different pre-clinical reports have demonstrated that luteolin has a large number of pharmacological exercises like enemy of hepatotoxic [37], hypotensive [38], hostile to urolithiasis [39], hemostatic [40], antimicrobial or antibacterial movement [41], and numerous others. It is seen that the luteolin has preventive action against a few parasitic specialists like Leishmania donovani [42] and plasmodium falciparum [43].

Drug-similarity and ADMET properties

We have done the virtual screening of medication similarity rules, and ADMET properties of Luteolin. Lipinski's standard, MDDR-like rule, Veber's standard, Ghose channel, Egan rule, Muegge rule, lipophilicity, water-solvency, and so on, are instances of medication resemblance rules [50]. A portion of the medication resemblance rules are sub-atomic weight < 500 g/mol, hydrogen bond contributors < 5, hydrogen bond acceptor < 10, MLOGP (n-octanol-water segment coefficient) < 4.15, molar refractivity ought to be somewhere in the range of 40 and 130, log P running between − 0.4 and + 5.6, dissolvability (log S) > − 5.7 [51]. Furthermore, retention, conveyance, digestion, discharge, and harmfulness (ADMET) properties are likewise significant in drug planning as they imply whether the compound goes through appropriate metabolic cycles in the human body or is poisonous [52]. In the current work, all the medication similarity and ADMET highlights are recorded with the assistance of the web-based data set SwissADME.

Forecast of cardiovascular poisonousness

Forecast of heart harmfulness distinguishes the cardio-related hurts by the utilization of the medication. Pred-hERG 4.2 is a uninhibitedly open approved web server that is utilized for the recognizable proof of cardiotoxic blockers of the compound [59]. The human ether-a go- related quality (hERG) is a cardiovascular repolarizer that principally encodes a protein and furthermore enacts the rectifier potassium channel (IKr) [60]. Heartbeat delay is the fundamental mindfulness of dysfunctioning of hERG which may frequently cause unexpected demise [61]. The design of luteolin is submitted to Pred-hERG in smileys design. Power, certainty, materialness space, and likelihood map are recorded as the outcomes [62]. To be non-cardio harmful, the certainty worth shouldn't surpass 0.26 for any compound [63]. The sections addressing hERG blockage are shown in the likelihood map.

Sub-atomic docking study

For sub-atomic docking studies, Chain 4 and Chain 7 are picked in view of the AGS cocrystal found normally in the CryoEM design of human MCM7 structure (PDB ID: 6XTX) [64]. Missing deposits in Chain 4 and 7 designs are finished utilizing SWISS-MODEL (https://swissmodel.expasy.org/). In view of the cocrystal AGS in the 6LXT design, the dynamic site not entirely set in stone as x: 211.170, y: 201.937, and z: 140.544, and the lattice box volume is picked as 20*20*20 Å3. Sub-atomic docking is performed with both Autodock Vina and Glide to approve the outcomes [65, 66]. The streamlined luteolin structure for atomic docking studies is gotten from the DFT study. The protein and ligand input pdbqt records expected for Autodock Vina docking are made with AutoDockTools- 1.5.6. For Glide docking, the protein structure is ready with the "Protein Preparation Wizard" in Schrödinger Maestro 12.8 and the ligand structure is ready with the "LigPrep" module utilizing OPLS4 force field. Protein-ligand communications are pictured utilizing BIOVIA Discovery Studio Visualizer v21 and UCSF Chimera v1.15 programming. The docked structure by Glide of Luteolin with chain 7 and chain 4 of 6XTX is additionally utilized for performing MD reproductions.

Sub-atomic elements reproductions

The product "Gromacs 2019.2 variant" is utilized for playing out the sub-atomic elements reenactment [67, 68]. The protein arrangement geography is made with Gromos 43A1 power field and SCP water model. The ligand geography record is acquired from the GlycoBioChem PRODRG2 server (http://davapc1.bioch.dundee.ac.uk/cgi-receptacle/prodrg) [69]. The protein-ligand complex is reproduced for 300 ps in accepted (measure of substance (N), pressure (P) and temperature (T) — NPT) and 300 ps isothermal-isobaric (measure of substance (N), volume (V), and balance steps temperature (T) — NVT) gatherings. The atomic elements reenactments run for 100 ns. The root mean square deviation (RMSD) and root mean square vacillation (RMSF)

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is determined to concentrate on the steadiness of the complex during the recreation. RMSD and RMSF help in the forecast of the nuclear positions and the complicated dependability of the particle going through reproduction.

III. RESULTS AND DISCUSSION.-

Cardiovascular poisonousness examination

The worth of the pertinence space for luteolin is seen to be 0.19 which lies in the OK reach (under 0.26). The likelihood map displayed in Fig. 6 demonstrates the presence of both positive and negative commitments of molecules or sections to the hERG blockage. From Fig. 6, it is observable that the pink-shaded area close to the OH bunches in the likelihood map demonstrates the diminished hERG blockage locale. The arrangement of iotas comprising oxygen advances the hERG heart possibility of the atom. The low worth of the pertinence space anticipated luteolin as non-cardiotoxic with a half certainty esteem.

IV. CONCLUSION-

This study has used extensive in-silico methods for deciding the counter malignant action of luteolin. The high worth of the dipole snapshot of the luteolin infers the bioactivity of the particle. Accordingly, it can more readily uphold the bond development between the medication and designated protein. Aftereffects of charge investigation show the property of charge move of the compound. FMO boundaries like ΔE, IP, EA, CP, and χ show values sufficiently good to legitimize its substance dependability in a perfect world. The high worth of η and the low worth of S show the firmness and the dependability of the atom. The presence of electrophilic and nucleophilic districts legitimizes the removal of the electron cloud and thus intermolecular charge move inside the luteolin atom. All through the virtual screening of pharmacokinetic properties like Lipinski rules, Ghose's channel, Egan's standard, Veber's standard, and Mugge's standard, and so on, luteolin substantiated itself a helpful compound that shows drug-like way of behaving. Alongside showing positive outcomes in ADMET properties, it answered PASS and cardio-harmful examination emphatically. The worth of dynamic likelihood for natural exercises is a lot higher than the dormant likelihood that approves the likelihood of organic exercises inside the particle. 0.19 is the incentive for the materialness space which is significantly less than 0.26 which is viewed as the cut-off incentive for cardio-poisonousness. In this manner, luteolin doesn't have any cardio-poisonous way of behaving and can be liked as an expected medication against MCM7 malignant growth. Moreover, the aftereffects of atomic docking uncovered the limiting score of the best restricting site is viewed as − 8.4 kcal/mol which is very great. The RMSD and RMSF values got by MD reproductions have demonstrated that the determination of docking present is by all accounts right. The amino corrosive buildups related to the limiting posture of the ligand with the protein changes over the reenactment time showing the point transformation in protein. It likewise conveys the accessibility of polar and nonpolar associations. The protein ligand complex keeps up with steadiness all through the reproduction time. Summing up all the in-silico concentrate on results coordinates toward areas of strength for the of Luteolin as an expected inhibitor. We accept that our current review would give a lead in drug improvement from luteolin for forestalling DNA replication.

REFERANCES-

[1]. Gupta SP. Quantitative structure- activity relationship studies on anticancer drugs. Chem Rev. 1994;94:1507–1551. doi: 10.1021/cr00030a003. [CrossRef] [Google Scholar]

[2]. Fu J, Zhou B, Zhang L, Balaji KS, Wei C, Liu X, Chen H, Peng J, Fu J. Expressions and significances of the angiotensin-converting enzyme 2 gene, the receptor of SARS-CoV-2 for COVID-19. Mol Biol Rep. 2020;47:4383–4392. doi: 10.1007/s11033-020-05478-4. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[3]. World Health Organisation health report on Cancer (2018) https://www.who.int/health-topics/cancer#:~:text=Cancer%20is%20the%20second%20leading,in%20six%20deaths%2C%20in%202018

[4]. IARC- GLOBOCAN (2020) New Global Cancer Data. https://www.uicc.org/news/globocan-2020-new-global-cancer

[5]. Nugent M. MicroRNA function and dysregulation in bone tumors: the

evidence to date. Cancer Manag Res. 2014;6:15–25. doi: 10.2147/CMAR.S53928. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[6]. Liu Y, Richards TA, Aves SJ (2009) Ancient diversification of eukaryotic MCM DNA replication proteins. BMC Evol Biol 9. 10.1186/1471-2148-9-60 [PMC free article] [PubMed]

[7]. Hua C, Zhao G, Li Y, Bie L. Minichromosome maintenance (MCM) family as potential diagnostic and prognostic tumor markers for human gliomas. BMC Cancer. 2014;14:526. doi: 10.1186/1471-2407-14-526. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[8]. Hyrien O (2016) How MCM loading and spreading specify eukaryotic DNA replication initiation sites. F1000Research 5 2063. 10.12688/f1000research.9008.1 [PMC free article] [PubMed]

[9]. Boos D, Frigola J, Diffley JFX. Activation of the replicative DNA helicase: breaking up is hard to do. Curr Opin Cell Biol. 2012;24:423–430. doi: 10.1016/j.ceb.2012.01.011. [PubMed] [CrossRef] [Google Scholar]

[10]. Donovan S, Harwood J, Drury LS, Diffley JFX. Cdc6p-dependent loading of Mcm proteins onto pre-replicative chromatin in budding yeast. PNAS. 1997;94:5611–5616. doi: 10.1073/pnas.94.11.5611. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[11]. Leman AR, Noguchi E. The replication fork: understanding the eukaryotic replication machinery and the challenges to genome duplication. Genes. 2013;4:1–32.

[12]. doi: 10.3390/genes4010001. [PMC free article] [PubMed] [CrossRef] [Google Scholar] 12. Petropoulou C, Kotantaki P, Karamitros D, Taraviras S. Cdt1 and Geminin in cancer: markers or triggers of malignant transformation. Front Biosci. 2008;13:4485–4494. doi: 10.2741/3018. [PubMed] [CrossRef] [Google Scholar]

[13]. Sen S, Chakraborty R, De B. Challenges and opportunities in the advancement of herbal medicine: India's position and role in a global context. J Herb Med. 2011;1:67–75. doi: 10.1016/j.hermed.2011.11.001. [CrossRef] [Google Scholar]

[14]. Lakhera S, Devlal K, Ghosh A, Rana M (2021) In silico investigation of phytoconstituents of medicinal herb piper longum against SARS-CoV-2 by molecular docking and molecular dynamics analysis. Results Chem 100199. 10.1016/j.rechem.2021.100199 [PMC free article] [PubMed]

[15]. Matulonis U, Sood A, Fallowfield L. Ovarian cancer. Nat Rev Dis Primers. 2016;2:16061. doi: 10.1038/nrdp.2016.61. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[16]. Duan Z, Wei B, Deng J, Mi Y, Dong Y, Zhu C, Fu R, Qu L, Fan D. The anti-tumor effect of ginsenoside Rh4 in MCF-7 breast cancer cells in vitro and in vivo. Biochem Biophys Res Commun. 2018;499:482–487. doi: 10.1016/j.bbrc.2018.03.174. [PubMed] [CrossRef] [Google Scholar]

[17]. Sadeghi S, Davoodvandi A, Pourhanifeh MH, Sharifi N, Nezhad RA, Sahebnasagh R, Moghadam SA, Sahebkar A, Mirzaei H. Anti-cancer effects of cinnamon: insights into its apoptosis effects. Eur J Med Chem. 2019;178:131–140.doi: 10.1016/j.ejmech.2019.05.067. [PubMed] [CrossRef] [Google Scholar]

[18]. Ambulkar S, Ambulkar P, Deshmukh MP, Budhrani AB (2020) Experimental evaluation of wound healing activity of various dosage forms of Tridax procumbens. Indian J Forensic Med Toxicol 14

[19]. Andriana Y, Xuan TD, Quy TN, Minh TN, Van TM, Viet TD. Antihyperuricemia, antioxidant, and antibacterial activities of Tridax procumbens L.". Foods. 2019;8:1–21.

[20]. doi: 10.3390/foods8010021. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[21]. Berlin Grace VM, Viswanathan S, David Wilson D et al (2020) Significant action of Tridax procumbens L. leaf extract on reducing the TNF-α and COX-2 gene expressions in induced inflammation site in Swiss albino mice. Inflammopharmacol 28:929–938. 10.1007/s10787-019-00634-0 [PubMed]

[22]. Bhagat V, Kondawar M (2019) Antitubercular potential of dendrophthoe

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 5 Sep-Oct 2022, pp: 563-569 www.ijprajournal.com ISSN: 2456-4494

falcate (l.) And Tridax procumbens (l.) Plants extracts against h37rv stain of mycobacteria tuberculosis. Int J Pharm Sci Res 10:251–259. 10.13040/IJPSR.0975-8232.10(1).251-59

[23]. Ravikumar V, Shivashangari KS, Devaki T (2005) Hepatoprotective activity of Tridax procumbens against d-galactosamine/lipopolysaccharide-induced hepatitis in rats. J Ethnopharmacol 101:55–60. 10.1016/j.jep.2005.03.019 [PubMed]

[24]. Bhagat VC, Kondawar MS. A comprehensive review on phytochemistry and pharmacological use of Tridax procumbens Linn. J pharmacogn phytochem. 2019;8:01–10. [Google Scholar]

[25]. Ikewuchi J. Effect of aqueous extract of Tridax procumbens Linn on plasma electrolytes of salt loaded rats, Pakistan. J Nutr. 2010;9:103–105. [Google Scholar]

[26]. Sujitha R, Sharmila R (2018) Phytochemical analysis and in vitro anticancer activity of Tridax procumbens linn. World J Pharm Res 7:867–878. 10.20959/wjpr201810-12319

[27]. Qiu Y, Wang W, Zhang B, Mei L, Shi Z. MCM7 amplification and overexpression promote cell proliferation, colony formation and migration in esophageal squamous cell carcinoma by activating the AKT1/mTOR signaling pathway. Oncol Rep. 2017;37:3590–3596. doi: 10.3892/or.2017.5614. [PubMed] [CrossRef] [Google Scholar]

[28]. Barik P, Talukdar P (2018) Established phytoligands from Tridax procumbens linn. Against bacterial dna-gyrase b receptor: molecular docking approach. World J Pharm Res 7. 10.20959/wjpr201812-12576

[29]. Imran M, Rauf A, Izneid TA, Nadeem M, Shariati MA, Khan IA, Imran A, Orhan IE, Rizwan M, Atif M, Gondal TA, Mubarak MS. Luteolin, a flavonoid, as an anticancer agent: a review. Biomed Pharmacother. 2019;112:108612. doi: 10.1016/j.biopha.2019.108612. [PubMed] [CrossRef] [Google Scholar]

[30]. Yu Q, Zhang M, Ying Q. Decrease of AIM2 mediated by luteolin contributes to non-small cell lung cancer treatment. Cell Death Dis. 2019;10:218. doi: 10.1038/s41419-019-1447-y. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[31]. Closas RG, Gonzalez CA, Agudo A, Riboli E. Intake of specific carotenoids and flavonoids and the risk of gastric cancer in Spain. Cancer Causes Control. 1999;10:71–75. doi: 10.1023/A:1008867108960. [PubMed] [CrossRef] [Google Scholar]

[32]. Rana M, Jain A, Rani V, Chowdhury P. Glutathione capped core/shell CdSeS/ZnS quantum dots as a medical imaging tool for cancer cells. Inorg Chem Commun. 2020;112:107723. doi: 10.1016/j.inoche.2019.107723. [CrossRef] [Google Scholar]

[33]. Fang J, Zhou Q, Shi XI, Jiang BH (2007) Luteolin inhibits insulin-like growth factor 1 receptor signaling in prostate cancer cells. Carcinogenesis 28:713–723. 10.1093/carcin/bgl189 [PubMed]

[34]. Ganai SA, Sheikh FA, Baba ZA, Mir MA, Mantoo MA, Yatoo MA. Anticancer activity of the plant flavonoid luteolin against preclinical models of various cancers and insights on different signalling mechanisms modulated. Phytother Res. 2021;35:3509–3532. doi: 10.1002/ptr.7044. [PubMed] [CrossRef] [Google Scholar]

[35]. Horinaka M, Yoshida T, Shiraishi T, Nakata S, Wakada M, Nakanishi R, Nishino H, Sakai T. The combination of TRAIL and luteolin enhances apoptosis in human cervical cancer HeLa cells. Biochem Biophys Res Commun. 2005;333:833–838. doi: 10.1016/j.bbrc.2005.05.179. [PubMed] [CrossRef] [Google Scholar]

[36]. Byun S, Lee KW, Jung SK, Lee EJ, Hwang MK, Lim SH, Bode AM, Lee HJ, Dong Z (2010) Luteolin inhibits protein kinase Cε and c-Src activities and UVB-induced skin cancer. Cancer Res 70. 10.1158/0008-5472.CAN-09-4093 [PubMed]

[37]. Khajuria R, Singh S, Bahl A (2019) General introduction and sources of flavonoids. In: Singh Tuli H. (eds) Current Aspects of Flavonoids: Their Role in Cancer Treatment, Springer, Singapore. 10.1007/978-981-13-5874-6_1

[38]. Wagh S, Shinde G. Protective effect of Tridax procumbens Linn against isoniazid induced hepatic damage. J Pharm Res.

2011;4:3612–3614. [Google Scholar]

[39]. Salahdeen HM, Yemitan OK, Alada ARA (2004) Effect of aqueous leaf extract of Tridax procumbens on blood pressure and heart rate in rats. Afr J Biomed Res 7. 10.4314/ajbr.v7i1.54062

[40]. Haytowitz DB, Bhagwat S, Holden JM. Sources of variability in the flavonoid content of foods. Procedia Food Sci. 2013;2:46–51. doi: 10.1016/j.profoo.2013.04.008. [CrossRef] [Google Scholar]

[41]. Lin Z, Fang Y, Huang A, Chen L, Guo S, Chen J (2014) Chemical constituents from Sedum aizoon and their hemostatic activity. Pharm Biol 52. 10.3109/13880209.2014.895019 [PubMed]