A Comprehensive Review on Exploration of Bioactive Phytoconstituents and Anti- Cancer potential of the Selected Fabaceae Species

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Abstract*—Cancer is the second leading cause of death worldwide, despite the availability of diverse treatment modalities such as surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapy. The limitations associated with these approaches including toxicity, drug resistance, and high costs have intensified the search for safer and more effective alternatives. In this context, phytochemicals have emerged as promising candidates for cancer prevention and therapy. These bioactive compounds exert anticancer effects through multiple mechanisms, including carcinogen inactivation, induction of cell cycle arrest, reduction of oxidative stress, stimulation of apoptosis, inhibition of angiogenesis, and modulation of immune responses. The family Fabaceae (Leguminosae) is the second largest and one of the most diverse families in the plant kingdom, with species widely distributed across tropical, subtropical, and temperate regions. Members of this family are rich sources of diverse phytochemicals such as flavonoids, lectins, saponins, alkaloids, carotenoids, and phenolic acids. These compounds have demonstrated a wide range of pharmacological activities, particularly anticancer potential, through antioxidant, anti-inflammatory, antiproliferative, and pro-apoptotic mechanisms. Despite the recognized therapeutic value of Fabaceae species, comprehensive exploration of their phytochemical profiles and anticancer mechanisms remains insufficient. Therefore, this review aims to consolidate and critically analyze the available information regarding the phytochemical composition of the Fabaceae family and their anticancer properties. Additionally, it highlights existing research gaps and proposes future directions to facilitate systematic investigation and translational development of Fabaceae derived anticancer agents.

***Index Terms*—Cancer; Phytochemicals; Fabaceae; Flavonoids; Apoptosis; Anticancer activity.**

I. INTRODUCTION

Cancer is a very dangerous disease and is characterized by the uncontrollable growth of cells. The number of cases and deaths due to cancer is increasing with every passing day. It is difficult to control and has become a major concern for scientists around the world [1]. Many stages (initiation, promotion, and progression) occur in the formation of the cancerous cells [2]. Irregular rates of dietary imbalance, hormonal imbalance, chronic infections, inflammation, and smoking are the major causes of cancer [3]. Despite several treatments to cure cancer, it is still considered the second most devastating cause of death around the world [4,5]. Various methods have been employed to treat cancer, e.g.,stem cell transplantation, chemotherapy, radiotherapy, immunotherapy, and surgery.

The most effective method to treat cancer is chemotherapy, but various side effects are associated with this method[6]. Due to the various side effects of radiotherapy and chemotherapy, alternative treatment methods with no or few side effects are required for the prevention and treatment of cancer [7]. Recently, researchers around the globe have focused their efforts on discovering novel drugs from natural sources such as plants with authentic medicinal importance [8]. Herbal treatment is a natural gift for humans to use to improve their health [9].Since ancient times, plants and their phyto-constituents have been used

as far as medicinal purposes are concerned [10]. Podophyllotoxin was discovered in the 1960s at the same time as when cancer treatments were being searched for from therapeutic plants, which contributed to the discoveries of taxol, vinblastine, camptothecin, and vincristine [11–13]. Many plants and their phytochemicals have the potential to control the spread of cancer in the body and continue to attract researchers to examine the anti-cancer activities of various extracted phytochemicals from plant sources [14].

Kingdom Plantae is characterized by approximately 250,000 plant species; however, the real issue is that only 10% of all plant species have been tested for the treatment of cancer. Anti-cancer compounds occur in various plant parts, e.g., leaf, flower, fruits, roots, stigmas, pericarp, embryo, rhizomes, seeds, stem, sprouts, and bark, and these phytochemicals are famous for their role in pharmacology. Different phytochemicals such as flavonoids, alkaloids, saponins, terpenes, lignin, vitamins, minerals, taxanes, gums, biomolecules, glycosides, oils, and various other metabolites are known to show anti-cancer activities. These compounds play a vital role in cancer prevention by activating enzymes and proteins, regulating cellular and signaling events in growth, their anti-inflammatory effect, and anti-oxidant action [15,16].

The Fabaceae family has a diverse fossil record where the late Paleocene period represents the oldest fossil records of the family, which shows the history of the Fabaceae family [17]. Most researchers believe that members of this family have evolved in arid and semiarid regions near the Tethys Sea [18].These plants have been the main part of meals in these regions since 6000 BC because of their richness in proteins. There is also a history of the use of these plants by humans in Asia, Europe, and North America for medicinal purposes [18,19]. Currently, species of the Fabaceae family occur naturally or are cultivated everywhere around the globe except the poles [18,20]. Different types of beans are used incuisines due to the irrichness of proteins and health-promoting activities in the Middle East, Asia, Mexico, and South America [20].

Phytochemicals of this family have industrial and pharmacological importance [21,22]. This family is a big source of phytochemicals, namely, flavonoids, lectins, saponins, alka- loids,carotenoids, and phenolicacids,which have an anti-cancer property,and th euse of these phytochemicals is increasing over time [23]. However, phytochemicals of this family have not been explored massively for their effect on cancer cell growth. Therefore, more research is needed in the future to explore the potential of phytochemicals of the Fabaceae family against cancer and to discover novel drugs against this disease. Various researchers have worked on anti-cancer aspects of the medicinal plants from the Fabaceae family. This review is the first attempt to explore the potential effects of phytochemicals of the Fabaceae family against cancer cell growth, development, and associated mechanisms. Moreover, research gaps have been explored and future recommendations are given.

II. PATHOGENESI OF CANCER AND PHYTOCHEMICAL ACTION

Various researches have been conducted over the passing time to understand the exact process of carcinogenesis. SpornandLi by [23] demonstrated that carcinogenesisis a multistep process, which is divided into three main phases, i.e., initiation, promotion, and finally progression. In most instances, a carcinogen is detoxified within the body as it enters. However, it may be activated through various metabolic pathways. According to Klaunig and Wang [24,25], carcinogenicagents increase oxidative stress and damage the DNA, and lead to the initiation of carcinogenesis. The proliferation activity of initiated cells starts during the promotion phase and leads to the preneoplastic cells' accumulation. These preneoplastic cells begin invading and spreading in different parts of the body during the third and the last phase, i.e., the progression phase. The progression phase is irreversible.[26].

The prevention and treatment of cancer by only one pathway does not turn out to be an effective way due to the involvement of multiple pathways in the occurrence as well as the progression of cancer [27,28].All the treatment strategies are subjected to a few hindrances, e.g.,side effects and drug resistance to chemotherapy [29]. These hindrances have made it difficult for scientists to efficiently develop various treatment strategies related to cancer [30,31]. Chemoprevention is an other approach that is widely

practiced worldwide, and it is useful during the initiation phase of carcinogenesis,while some have even reported its effectiveness in the promotion and progression phases too [32].

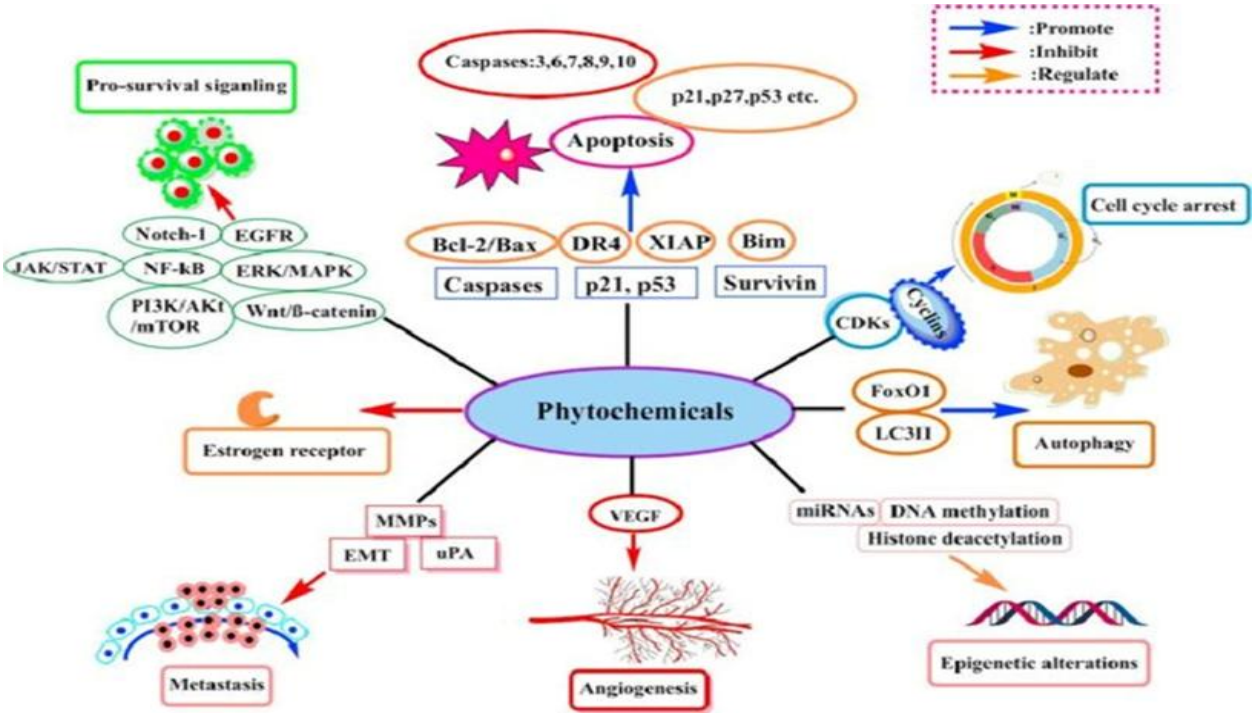

Figure 1:.Phytochemicals'pathway of anti-cancer effect.

The chemopreventive agents are generally classified into two principal categories, where one group includes blocking agents, while others are suppressive agents majorly sourced from plant phytochemicals [33]. Blocking agents work uniquely; they suppress the carcinogen activation through the metabolic pathway and do not allow carcinogenic agents to interact with the biomolecule. On the other hand, suppressive agents work in another way and suppress the promotion or progression of cancerous cells [34].The chemopreventive agents usually have an anti-proliferative and anti-oxidant effect or regulate specific enzyme activities and cell cycles. Furthermore, these agents also regulate signal transduction pathways and prevent carcinogenesis [35]. The phytochemicals' pathway of the anti-cancer effect is presented in Figure 3.

III. DEVELOPMENT OF PHYTOCHEMICAL DRUGS FROM THE MEDICINAL PLANTS

The therapeutic potential of plants largely depends on the quality and concentration of their active phytochemicals. Several factors influence phytochemical composition, including the plant's age, environmental conditions, climate, and seasonal variations. Moreover, different plant parts often vary in their levels of bioactive constituents, with some tissues accumulating higher concentrations than others. Despite considerable progress, further research is necessary to deepen our understanding of phytochemicals and to better exploit their role in cancer prevention and treatment. A variety of techniques are available for the purification and identification of active phytochemicals, such as isolation assays, combinatorial chemistry, and bioassay-guided fractionation. These methods facilitate the detection, characterization, and development of biologically active compounds for therapeutic applications. [35].

Several analytical methods are employed to separate bioactive compounds from complex mixtures during bioassay-guided fractionation. The process typically begins with the preparation and biological evaluation of natural extracts obtained from either dry or fresh plant materials [36]. Once biological activity is confirmed, the active extract undergoes fractionation using suitable stationary matrices.

A range of analytical techniques—including mass spectrometry (MS), high-performance liquid chromatography (HPLC), thin-layer chromatography (TLC), Fourier-transform infrared spectroscopy (FTIR), and nuclear magnetic resonance (NMR) spectroscopy—are utilized for the separation and characterization of active constituents. Various solvents are selected based on the polarity and chemical nature of the compounds. For chromatographic fractionation, matrices such as silica gel, Superdex, and other appropriate materials are commonly used. In addition, specific dyes and detecting reagents assist in the visualization and identification of bioactive phytochemicals in medicinal plants.[37]

Following purification, isolated phytochemicals are evaluated for their anticancer potential through in vitro and in vivo studies. Upon demonstrating significant anticancer activity, further investigations focus on critical parameters such as pharmacokinetics, metabolic pathways, adverse effects, immunogenicity, pharmacodynamics, dose optimization, and potential drug interactions. These aspects are essential for the rational design and development of novel anticancer agents [38].

IV. MAJOR PHYTOCHEMICAL CONSTITUENTS OF THE FABACEAE FAMILY

Species of the Fabaceae family are vital sources of phytochemicals, including flavonoids, lectins, saponins, alkaloids, carotenoids, and phenolic acids. These phytochem-icals are present in every genus of the Fabaceae family and possess great medicinal values [18,22]. The phytochemicals have gained considerable recognition as far as anticancer properties are concerned [13]. However, the phytochemicals of the Fabaceae family have not been explored by various researchers around the world. According to available data, all these phytochemicals have significant anti-cancer values against different forms of cancers in humans. The structures of different phytochemicals found in different members of the Fabaceae family represented in Figure 6.

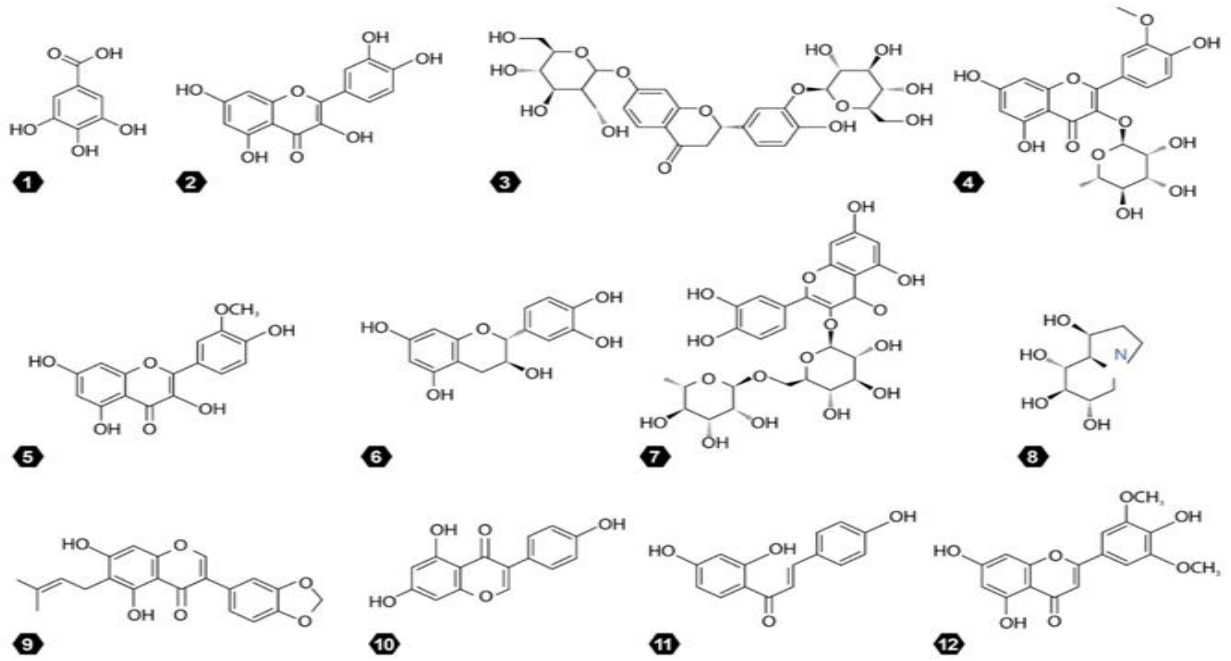

Figure 6. Structure of main phytochemicals from family Fabaceae. 1.Gallicacid. 2.Quercetin. 3.Butrin. 4.Isorhamnetin-3-O-rhamnoside.5. Isorhamnetin.6. Catechin.7. Rutin.8. Castanosper-mine. 9.Derrubone.10. Genistein.11. Isoliquiritigenin.12. Tricin.

Flavonoids

Flavonoids are considered to be effective anti-oxidants and are known to exhibit anti- angiogenic activity.Various studies have reported that flavonoids inhibit the metabolic activation of carcinogens and

stop the further growth of abnormal cells, which may de-velop into cancerous cells [36]. Flavonoids and their derivatives are considered the vital phytochemical constituents of the Fabaceae family. The most important flavonoids isolated from the various members of the family are chalcone, flavones, flavonol, isoflavones, a flavonol glycoside, prenylated flavonoids, and lavandulyl flavanones [37]. According to Krishna et al. [38], prenylated flavonoids from various members of the Fabaceae family are known to exhibit anti-oxidant and anti-cancer activities.

Lectins

Most members of the Fabaceae family are rich in lectin proteins, and communities invariousregionsusetheseplantsfordifferentdiseasesduetotheiranti-cancerandanti- tumor activities [39].Several studies have confirmed the tumor inhibition mechanisms of lectins in various cell lines including bone, skin, bile duct, and liver cell lines [40–45]. According to De Mejia and Prisecaru [46], various forms of lectins showed anti-cancer properties under in vivo and invitro conditions. Lectins bind with cancer cell membranes or their receptors resulting in apoptosis and cytotoxicity, and finally suppress the cancer cell growth. Fang et al. [47] assessed the anti-cancer activity of lectin isolated from the *Phaseolus vulgaris* L. and declared that lectin possesses anti-cancer activities, particularly against MCF-7, nasopharyngeal carcinoma cells (HNE-2, CNE-1, CNE-2), and liver cancer cells (HepG2). Moreover, *P.vulgaris* lectin regulates nitricoxide (NO) production through the up regulation of inducible NO synthase known to introduce apoptotic bodies and contribute totheanti-carcinogenic activity. Simila results were confirmed by Lamand Ng[48] while working on the anti-cancer propertie so flectinisolated from *P.vulgaris*.

Saponins

Several members of the Fabaceae family including peanut, soybean, and lentilare rich in saponins and reported to exhibit anti-cancer properties. Various researchers around the globe have confirmed that saponins isolated from members of the Fabaceae family are effective against colon cancer, melanoma cells, and cervical cancer. Saponins can follow various mechanisms to suppress the progression of cancer by cell cycle arrest, the inhibition of cellular invasion, anti-oxidant activity, and the induction of autophagy and apoptosis [49]. Rochfort and Panozzo [50] stated that the intake of legume saponins enhances the immunity against various types of cancer including cervical and colon cancer. Mudryj et al. [51] examined the anti-carcinogenic activity of legume saponins and reported that saponins involve different mechanisms such as immune modulatory effects, acid and neutral sterol metabolism, the normalization of carcinogen-induced cell proliferation, and cytotoxicity of cancerous cells.[52]

Alkaloids

Alkaloids are vital secondary metabolites that are considered a valuable source of novel drugs. Several studies have confirmed that alkaloids have anti-cancer and anti- proliferative properties [53,54,55]. Vindesine, vinorelbine, vinblastine, and vincristine are the best examples of alkaloids, which have already been successfully developed as anti-cancer drugs. These are effective against different forms of cancer including testicular cancer, brain cancer, lung cancer, bladder cancer, and melanoma. Over 21,000 different alkaloids have been identified and most of these alkaloids are a great source of medicines, especially exhibiting anti-cancer activities [56,57].

Carotenoids

Legume leaves are a vital source of carotenoids, which primarily include carotenes, while other carotenoids are lutein, neoxanthin, crocetin, antheraxanthin, violaxanthin, and some others in a very low quantity. On the other hand, legume roots are not as rich in carotenoids as the leaves [58].Many experimental studies have identified various mechanisms through which carotenoids may control the development tof various types of cancer in humans. These mechanisms include anti-oxidant actions, retinol, communication functions, and cell signaling. Therefore, anti-oxidant defense support from the carotenoids reduces cancer risks [59]. Nishino et al. [60] carried out an extensive study and reported that β-carotene, β-cryptoxanthin, lycopene, lutein, and zeaxanthin can be use daschemo-preventative agents. Moreover, beta-cryptoxanthin regulates the expression of the RB gene, which is a known anti-oncogene.[61] Horvathetal.[62] stated that the carotenoids extracted from legumes have protective, preventative, and even curative effects against various types of cancer.[63]

Phenolic Acids

Phenolicacids are vital phytochemicals present in considerable amounts in the members of the Fabaceae family. Phenolic acids are non-flavonoid phenolic compounds that occurin the free, insoluble-bound, and conjugated soluble forms. On the otherhand, these non-flavonoid phenolic compounds are widely distributed in plant species[64]. Natural phenolic acids present in various members of the Fabaceae family are ferulicacid, vanillic acid, caffeicacid, benzoicacid, p-hydroxyacid,3,4-dihydroxybenzoicacid,sinapinicacid and syringic acid [65]. Phenolic acids are secondary compounds that have been explored recently against various diseases, particularly cancer. These phenolics reduce the prolifera- tion of cancerous cells, promote apoptosis, and target various aspects of cancer including growth, development, and metastasis [66]. Recently, phenolic acids have been extensively studied due to their anti-inflammatory, anti-tumor, and anti-oxidant activities [67]. Anan- tharajuetal.[68] demonstrated that the anti-carcinogenic effect of phenolicacids is largely due to five activities: (1) modulation of ROS levels, (2) inducing cell cycle arrest, (3) promoting the suppression of tumor proteins such as p53, (4) suppressing oncogenic signaling cascades controlling apoptosis and angiogenesis as well as proliferation, (5) increasing the ability to differentiate and, finally, transforming into normal cells.[69,70].

V. CONCLUSIONS AND FUTURE DIRECTIONS

Species belonging to the Fabaceae family are recognized as abundant sources of diverse phytochemicals, including flavonoids, lectins, saponins, alkaloids, carotenoids, and phenolic acids.[71] The consumption of various Fabaceae species has been associated with a reduced risk of cancer, largely due to the chemopreventive and therapeutic potential of their bioactive constituents.[72] Several of these phytochemicals are already being utilized in anticancer strategies worldwide, while many others are increasingly gaining scientific attention. Phytochemicals derived from Fabaceae plants exert anticancer effects through multiple mechanisms, such as carcinogen inactivation, induction of cell cycle arrest, attenuation of oxidative stress, promotion of apoptosis, and modulation of immune responses.[73] Nevertheless, extensive research is still required to comprehensively evaluate the anticancer potential of Fabaceae phytoconstituents.[74] Additional data on their bioactivity could facilitate the discovery and development of novel anticancer agents. Future investigations should also focus on elucidating the precise molecular mechanisms underlying their anticancer effects.[75] Although individual phytochemicals have demonstrated promising activity, the possible synergistic interactions among multiple bioactive compounds within a single plant species remain insufficiently explored.[76] Furthermore, long-term safety profiles, including potential physiological alterations associated with prolonged use of these compounds, need thorough evaluation.[77] Despite numerous reports supporting the anticancer efficacy of Fabaceae-derived phytochemicals, most findings are limited to in vitro and in vivo experimental models, with relatively few well-designed clinical trials available.[78] Therefore, robust clinical investigations are essential to validate their therapeutic efficacy and clarify their mechanisms of action.[79] To meet international standards, systematic standardization is also required, including validated analytical methods for assessing bioavailability, efficacy, safety, quality control, compositional consistency, manufacturing practices, and compliance with regulatory approval requirements.[80]

REFERENCES

[1] Saini, A.; Kumar, M.; Bhatt, S.; Saini, V.; Malik, A. Cancer causes and treatments. Int. J. Pharm. Sci. Res. 2020, 11, 3121–3134.

[2] Subramaniam, S.; Selvaduray, K. R.; Radhakrishnan, A. K. Bioactive compounds: Natural defense against cancer. Biomolecules 2019, 9, 758.

[3] Gezici, S.; Sekeroglu, N. Current perspectives in the application of medicinal plants against cancer: novel therapeutic agents. Anti-Cancer Agents in Medicinal Chemistry 2019, 19, 101–111.

[4] Iqbal, J.; Abbasi, B. A.; Mahmood, T.; Kanwal, S.; Ali, B.; Shah, S. A.; Khalil, A. T. Plant-derived anticancer agents: A green anticancer approach. Asian Pac. J. Trop. Biomed. 2017, 7, 1129–1150.

[5] Mattiuzzi, C., Lippi, G. Current cancer epidemiology. J. Epidemiol. Glob. Health, 2019, 9, 217.
[6] Cid-Gallegos, M.S.; Sánchez-Chino, X.M.; Juárez Chairez, M.F.; Álvarez González, I.; Madrigal-Bujaidar, E.; Jiménez-Martínez, C. Anticarcinogenic activity of phenolic compounds from sprouted legumes. Food Rev. Int. 2020, 2020, 1184058.
[7] Rizeq, B.; Gupta, I.; Ilesanmi, J.; AlSafran, M.; Rahman, M.M.; Ouhtit, A. The power of phytochemical combinations in cancer chemoprevention. J. Cancer 2020, 11, 4521.
[8] Harvey, A.L. Natural products in drug discovery. DrugDiscov. 2008, 13, 894–901.
[9] Zhang, J.; Hu, K.; Di, L.; Wang, P.; Liu, Z.; Zhang, J.; Yue, P.; Song, W.; Zhang, J.; Chen, T.; et al. Traditional herbal medicine and nanomedicine: Converging disciplines to improve therapeutic efficacy and human health. Adv. Drug Deliv. Rev. 2021, 178, 113964.
[10] Usman, M.; Ditta, A.; Ibrahim, F.H.; Murtaza, G.; Rajpar, M.N.; Mehmood, S.; Saleh, M.N.B.; Imtiaz, M.; Akram, S.; Khan, W.R. Quantitative ethnobotanical analysis of medicinal plants of high-temperature areas of Southern Punjab, Pakistan. Plants 2021, 10, 1974.
[11] Thakore, P.; Mani, R.K.; Kavitha, S.J. A brief review of plants having anti-cancer properties. Int. J. Pharm. Res. Dev. 2012, 3, 129–136.
[12] Tariq, A.; Sadia, S.; Pan, K.; Ullah, I.; Mussarat, S.; Sun, F.; Abiodun, O. O.; Batbaatar, A.; Li, Z.; Song, D.; et al. A systematic review of ethnomedicines of anti-cancer plants. Phytother. Res. 2017, 31, 202–264.
[13] Sebastian, R.; Jaykar, B.; Gomathi, V. Current status of anticancer research in the Fabaceae family. Pathways 2020.
[14] Samec, M.; Liskova, A.; Koklesova, L.; Samuel, S. M.; Murin, R.; Zubor, P.; Bujnak, J.; Kwon, T. K.; Büsselberg, D.; Prosecky, R.; et al. The role of plant-derived natural substances as immunomodulatory agents in carcinogenesis. J. Cancer Res. Clin. Oncol. 2020, 146, 3137–3154.
[15] Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global cancer statistics 2020: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 2021, 71, 209–249.
[16] Thomas, R.; Butler, E.; Macchi, F.; Williams, M. Phytochemicals in cancer prevention and management. Br. J. Med. Pract. 2015, 8, 1–8.
[17] Sharma, A.; Kaur, R.; Katnoria, J.K.; Kaur, R.; Nagpal, A.K. Family Fabaceae: A boon for cancer therapy. In Biotechnology and Production of Anti-Cancer Compounds; Malik, S., Ed.; Springer: Cham, Switzerland, 2017; pp. 157–175.
[18] Schrire, B. A review of the tribe Indigofereae (Leguminosae–Papilionoideae) in Southern Africa (including South Africa, Lesotho, Swaziland & Namibia; excluding Botswana). S. Afr. J. Bot. 2013, 89, 281–283.
[19] Messina, M.J. Legumes and soybeans: Overview of their nutritional profiles and health effects. Am. J. Clin. Nutr. 1999, 70, 439s–450s.
[20] Pastorino, G.; Cornara, L.; Soares, S.; Rodrigues, F.; Oliveira, M.B.P. Liquorice (Glycyrrhiza glabra): A phytochemical and pharmacological review. Phytother. Res. 2018, 32, 2323–2339.
[21] Batiha, G.E.S.; Beshbishy, A.M.; El-Mleeh, A.; Abdel-Daim, M.M.; Devkota, H.P. Traditional uses, bioactive chemical constituents, and pharmacological and toxicological activities of Glycyrrhiza glabra L. (Fabaceae). Biomolecules 2020, 10, 352.
[22] El-Feky, A.M.; Elbatanony, M.M.; Mounier, M.M. Anti-cancer potential of the lipoidal and flavonoidal compounds from Pisum sativum and Vicia faba peels. Egypt.J.BasicAppl.Sci.2018,5,258–264.
[23] Sporn, M.B.; Liby, K.T. Chemoprevention of Cancer: Past, Present, and Future. In Natural Products for Cancer Chemoprevention; Springer: Berlin/Heidelberg, Germany, 2020; pp. 1–18.
[24] Dandawate, P.; Ahmad, A.; Deshpande, J.; Swamy, K.V.; Khan, E.M.; Khetmalas, M.; Padhye, S.; Sarkar, F. Anticancer phytochemical analogs 37: Synthesis, characterization, molecular docking, and cytotoxicity of novel plumbagin hydrazones against breast cancer cells. Bioorganic Med. Chem. Lett. 2014, 24, 2900–2904.
[25] Ranjan, A.; Ramachandran, S.; Gupta, N.; Kaushik, I.; Wright, S.; Srivastava, S.; Das, H.; Srivastava, S.; Prasad, S.; Srivastava, S.K. Role of phytochemicals in cancer prevention. Int.J.Mol.Sci.2019,20,4981.
[26] Nedeljkovic, M.; Damjanovic, A. Mechanisms of chemotherapy resistance in triple-negative breast cancer—How we can rise to the challenge. Cells 2019, 8, 957.
[27] Meguid, R.A.; Hooker, C.M.; Taylor, J.T.; Kleinberg, L.R.; Cattaneo, S.M., II; Sussman, M.S.; Yang, S.C.; Heitmiller, R.F.; Forastiere, A.A.; Brock, M.V. Recurrence after neoadjuvant chemoradiation and surgery for esophageal cancer: Does the pattern of recurrence differ for patients with a complete response and those with partial or no response? J.Thorac.Cardiovas c. Surg. 2009, 138, 1309–1317.

[28] Chan, C.W.; Law, B.M.; So, W.K.; Chow, K.M.; Waye, M.M. Novel strategies on personalized medicine for breast cancer treatment: An update. Int. J. Mol. Sci. 2017, 18, 242 3.
[29] Koh, Y.C.; Ho, C.T.; Pan, M.H. Recent advances in cancer chemop J. Food Drug Anal. 2020, 28, 14–37.
[30] Dewanjee, S.; Das, S.; Joardar, S.; Bhattacharjee, S.; Chakraborty, P. Carotenoids as Anticancer Agents. In Carotenoids: Structure and Function in the Human Body; Springer: Berlin/Heidelberg, Germany, 2021; p. 475.
[31] Iqbal, J.; Abbasi, B. A.; Ahmad, R.; Batool, R.; Mahmood, T.; Ali, B.; Khalil, A. T.; Kanwal, S.; Shah, S. A.; Alam, M. M.; et al. Potential phytochemicals in the fight against skin cancer: Current landscape and future perspectives. Biomed. Pharmacother. 2019,109,1381–1393.
[32] Steward, W. P.; Brown, K. Cancer chemoprevention: A rapidly evolving field. Br. J. Cancer 2013, 109, 1–7.
[33] Hassan, L.E.A.; Ahamed, M.B.K.; Majid, A.S.A.; Baharetha, H.M.; Muslim, N.S.; Nassar, Z.D.; Majid, A.M.A. Correlation of antiangiogenic, antioxidant, and cytotoxic activities of some Sudanese medicinal plants with phenolic and flavonoid contents.BMCComplement. Med. Ther. 2014, 14,406.
[34] Agbo, M.O.; Uzor, P.F.; Nneji, U.N.A.; Odurukwe, C.U.E.; Ogbatue, U.B.; Mbaoji, E.C. Antioxidant, total phenolic, and flavonoid content of selected Nigerian medicinal plants. Dhaka Univ. J. Pharm. Sci. 2015, 14, 35–41.
[35] Krishna, P.M.; KNV, R.; Banji, D. A review on phytochemical, ethnomedical, and pharmacological studies on genus Sophora, Fabaceae. Rev. Bras. Farmacogn. 2012, 22, 1145–1154.
[36] Fu, L.L.; Zhou, C.C.; Yao, S.; Yu, J.Y.; Liu, B.; Bao, J.K. Plant lectins: Targeting programmed cell death pathways as antitumor agents. Int. J. Biochem. Cell Biol. 2011, 43, 1442–1449.
[37] Gautam, A.K.; Shrivastava, N.; Sharma, B.; Bhagyawant, S.S. Current scenario of legume lectins and their practical applications. J. Crop Sci. Biotechnol. 2018, 21, 217–227.
[38] Bhutia, S.K.; Panda, P.K.; Sinha, N.; Praharaj, P.P.; Bhol, C.S.; Panigrahi, D.P.; Mahapatra, K.K.; Saha, S.; Patra, S.; Mishra, S.R.; et al. Plant lectins in cancer therapeutics: Targeting apoptosis and autophagy-dependent cell death. Pharmacol. Res. 2019, 144, 8–18.
[39] Majeed, M.; Hakeem, K. R.; Rehman, R. U. Mistletoe Lectins: From Interconnecting Proteins to Potential Tumor-Inhibiting Agents. Phytomed. Plus 2021, 1, 100039.
[40] DeMejia, E.G.; Prisecaru, V.I. Lectins as bioactive plant proteins: A potential in cancer treatment. Crit. Rev. Food Sci. Nutr. 2005, 45, 425–445.
[41] Gautam, A.K.; Gupta, N.; Narvekar, D.T.; Bhadkariya, R.; Bhagyawant, S.S. Characterization of chickpea (Cicer arietinum L.) lectin for biological activity. Physiol. Mol. Biol. Plants 2018, 24, 389–397.
[42] Cavada, B.S.; Silva, M.T.L.; Osterne, V.J.S.; Pinto-Junior, V.R.; Nascimento, A.P.M.; Wolin, I.A.V.; Heinrich, I.A.; Nobre, C.A.S.; Moreira, C.G.; Lossio, C.F.; et al. Canavalia bonariensis lectin: Molecular bases of glycoconjugate interaction and antiglioma potential. Int. J. Biol. Macromol. 2017, 106, 369–378.
[43] Arteaga, I.T.; Guillen, J.C.; Olaya, E.M.; Gasca, T.G.; Zaragoza, M.V.Á.; García-Santoyo, V.; Castillo, J.T.; Aguirre, C.; Phinney, B.; Blanco-Labra, A. Characterization of two non-fetuin-binding lectins from tepary bean (Phaseolus acutifolius) seeds with differential cytotoxicity on colon cancer cells. J. Glycobiol. 2016, 5, 1–7.
[44] Mujoo, K.; Haridas, V.; Hoffmann, J. J.; Wächter, G. A.; Hutter, L. K.; Lu, Y.; Blake, M. E.; Jayatilake, G. S.; Bailey, D.; Mills, G. B.; et al. Triterpenoid saponins from Acacia victoriae (Bentham) decrease tumor cell proliferation and induce apoptosis. Cancer Res. 2001, 61, 5486–5490.
[45] Kavitha, C.N.; Raja, K.D.; Rao, S.K. Antitumor activity of Albizia lebbeck L. against Ehrlich ascites carcinoma in vivo and HeLa and A549 cell lines in vitro. J. Cancer Res. Ther. 2021, 17,491.
[46] Melek, F.R.; Aly, F.A.; Kassem, I.A.; Abo-Zeid, M.A.; Farghaly, A.A.; Hassan, Z.M. Three further triterpenoid saponins from Gleditsia caspica fruits and the protective effect of the total saponin fraction on cyclophosphamide-induced genotoxicity in mice. Z. Naturforsch. C2015, 70, 31–37.
[47] Nayeem, N.; Imran, M.; Asdaq, S.M.B.; Rabbani, S.I.; Alanazi, F.A.; Alamri, A.S.; Sampaio, M.U.; Jochum, M.; Oliva, M.L.V. Total phenolic,flavonoid contents,and biological activities of stem extracts of Astragalus spinosus (Forssk.) Mushrooms grown in Northern Border Province, Saudi Arabia. SaudiSci.J.Biol.Sci.2022,29,1277–1282.
[48] Zhou, R.; Chen, H.; Chen, J.; Chen, X.; Wen, Y.; Xu, L. Extract from Astragalus membranaceus inhibits breast cancer cell proliferation via the

PI3K/AKT/mTOR signaling pathway. BMC Complement Altern Med. 2018, 18, 83.
[49] Sebastian, D.; Shankar, K. G.; Ignacimuthu, S.; Sophy, A. R.; Vidhya, R.; Anusha, J. R. Bauhinia acuminata L. attenuates lung cancer cell proliferation: In vitro, in vivo, and in silico approaches. Phytomed. Plus 2022, 2, 100173.
[50] Ullah, A.; Munir, S.; Badshah, S.L.; Khan, N.; Ghani, L.; Poulson, B.G.; Emwas, A.H.; Jaremko, M. Important flavonoids and their role as a therapeutic agent. Molecules2020,25,5243.
[51] Agrawal, S. B.; Gupta, N.; Bhagyawant, S. S.; Gaikwad, S. M. Anticancer activity of lectins from Bauhinia purpurea and Wisteria floribunda on breast cancer MCF-7 cell lines. ProteinPept.Lett.2020, 27, 870–877.
[52] Osman, S.M.; Khalek, S.M.A.; Koheil, M.A.; El-Haddad, A.E.; Wink, M. A new steroidal compound (β-sitosterol-3-O-butyl) isolated from Caesalpinia gilliesii flowers. Int. J. Appl. Res. Nat. Prod. 2015, 8, 14–19.
[53] Zanin, J.L.; Massoni, M.; Santos, M.H.D.; Freitas, G.C.D.; Niero, E.L.; Schefer, R.R.; Lago, J.H.; Ionta, M.; Soares, M.G. Caesalpinioflavone, from Caesalpinia pluviosa var. peltophoroides. J. Braz. Chem. Soc. 2015, 26, 804–809.
[54] Bhagat, M.; Saxena, A. K. Evaluation of Cassia occidentalis for in vitro cytotoxicity against human cancer cell lines and antibacterial activity. IndianJ.Pharmacol.2010,42,234.
[55] Taiwo, F.O.; Akinpelu, D.A.; Aiyegoro, O.A.; Olabiyi, S.; Adegboye, M.F. The biocidal and phytochemical properties of leaf extract of Cassia occidentalis Linn. Afr. J. Microbiol. Res. 2013, 7, 3435–3441.
[56] Kato, A.; Hirokami, Y.; Kinami, K.; Tsuji, Y.; Miyawaki, S.; Adachi, I.; Hollinshead, J.; Nash, R.J.; Kiappes, J.L.; Zitzmann, N.; et al. Isolation and SAR studies of bicyclic iminosugars from Castanospermum australe as glycosidase inhibitors. Phytochemistry 2015, 111, 124–131.
[57] Bouziane, A.; Bakchiche, B.; Dias, M.I.; Barros, L.; Ferreira, I.C.; AlSalamat, H.A.; Bardaweel, S.K. Phenolic Compounds and Bioactivity of Cytisus villosus Pourr. Molecules 2018, 23, 1994.
[58] Ito, C.; Matsui, T.; Miyabe, K.; Hasan, C. M.; Rashid, M. A.; Tokuda, H.; Itoigawa, M.Three is of lavones from Derris scandens (Roxb.) Benth and their cancer chemopreventive activity and in vitro antiproliferative effects. Phytochemistry 2020, 175, 112376.
[59] Fofana, S.; Ouédraogo, M.; Esposito, R. C.; Ouedraogo, W. P.; Delporte, C.; Van Antwerpen, P.; Mathieu, V.; Guissou, I. P. Systematic Review of Potential Anticancerous Activities of Erythrina senegalensis DC (Fabaceae). Plants 2021, 11, 19.
[60] Mohammed, R.S.; Abou Zeid, A.H.; El Hawary, S.S.; Sleem, A.A.; Ashour, W.E. Flavonoid constituents, cytotoxic and antioxidant activities of Gleditsia triacanthos L. leaves. Saudi J. Biol. Sci. 2014, 21, 547–553.
[61] Cai, Y.; Zhang, C.; Zhan, L.; Cheng, L.; Lu, D.; Wang, X.; Xu, H.; Wang, S.; Wu, D.; Ruan, L. Anticancer effects of Gleditsia sinensis extract in rats transplanted with hepatocellular carcinoma cells. Oncol. Res. 2019, 27, 889.
[62] Jung, S.K.; Lee, M.H.; Kim, J.E.; Singh, P.; Lee, S.Y.; Jeong, C.H.; Lim, T.G.; Chen, H.; Chi, Y.I.; Kundu, J.K.; et al. Isoliquiritigenin induces apoptosis and inhibits xenograft tumor growth of human lung cancer cells by targeting both wild-type and L858R/T790M mutant EGFR. J. Biol. Chem. 2014, 289, 35839–35848.
[63] Mohamed, K.M.; Salwa, B.E.M.; Nadia, T.S.; Eshak, M.E.H.; Heba, A.B. Study of antioxidants and anticancer activity of licorice [Glycyrrhiza glabra] extracts. Egypt. J. Nutri. 2008, 23, 177–203.
[64] Srinivasan, S.A.; Wankhar, W.A.; Rathinasamy, S.H.; Rajan, R.A. Larvicidal potential of Indigofera tinctoria (Fabaceae) on dengue vector (Aedes aegypti) and its antimicrobial activity against clinical isolates. Asian J. Pharm. Clin. Res. 2015, 8, 316–319.
[65] Vijayan, R.; Joseph, S.; Mathew, B. Indigofera tinctoria leaf extract mediated green synthesis of silver and gold nanoparticles and assessment of their anticancer, antimicrobial, antioxidant, and catalytic properties. Artif.CellsNanomed. Biotechnol. 2018, 46, 861–871.
[66] Ramya, V.; Madhu-Bala, V.; Prakash-Shyam, K.; Gowdhami, B.; Sathiya-Priya, K.; Vignesh, K.; Vani, B.; Kadalmani, B. Cytotoxic activity of Indigofera aspalathoides (Vahl.) extracts in cervical cancer (HeLa) cells: Ascorbic acid adjuvant treatment enhances the activity. Phytomed. Plus 2021, 1, 100142.
[67] ElHafeez, A.; Ali, A.; Khalifa, H. O.; Elgawish, R. A.; Shouman, S. A.; ElTwab, A.; Hussein, M.; Kawamoto, S. Melilotus indicus extract induces apoptosis in hepatocellular carcinoma cells via a mechanism involving mitochondria-mediated pathways. Cytotechnology 2018, 70, 831–842.
[68] Chanu, K.V.; Leishangthem, G.D.; Srivastava, S.K.; Thakuria, D.; Kataria, M.; Telang, A.G. Phytochemical analysis and evaluation of the anticancer activity of Parkia javanica seeds. Pharm. Innov. 2018, 7, 305.

[69] Pfitzinger, P.L.; Fangmann, L.; Mundt, B.; Brooks, J.; D'Haese, T.; Teller, S.; Hecker, A.; et al. Indirect cholinergic activation slows down pancreatic cancer growth and tumor-associated inflammation. J. Exp. Clin. Cancer Res. 2020, 39, 289.

[70] Raghavendra, M.P.; Satish, S.; Raveesha, K.A. Alkaloids Isolated from Leaves of Prosopis juliflora against Xanthomonas pathovars.Arch.Phytopathol.Plant.Prot.2009,42,1033–1041.

[71] Henciya, S.; Seturaman, P.; James, A. R.; Tsai, Y. H.; Nikam, R.; Wu, Y. C.; Dahms, H. U.; Chang, F. R. Biopharmaceutical potential of Prosopis spp. (Mimosaceae, Leguminosa). J. Food Drug Anal. 2017, 25, 187–196.

[72] Asati, V.; Srivastava, A.; Mukherjee, S.; Sharma, P. K. Comparative analysis of antioxidant and antiproliferative activities of crude and purified flavonoid-enriched fractions of pods/seeds of two desert legumes. Prosopis cineraria and Cyamopsis tetragonoloba. Heliyon 2021, 7, e07304.

[73] Cai, Y.Z.; Sun, M.; Xing, J.; Luo, Q.; Corke, H. Structure–radical scavenging activity relationships of phenolic compounds from traditional Chinese medicinal plants. LifeSci. 2006, 78, 2872–2888.

[74] Chen, H.; Zhang, J.; Luo, J.; Lai, F.; Wang, Z.; Tong, H.; Lu, D.; Bu, H.; Zhang, R.; Lin, S. Antiangiogenic effect of oxymatrine on pancreatic cancer by inhibition of the NF-κB-mediated VEGF signaling pathway. Oncol. Rep. 2013, 30, 589–595.

[75] Liu, Y.; Bi, T.; Dai, W.; Wang, G.; Qian, L.; Gao, Q.; Shen, G. RETRACTED: Effectsofoxymatrineontheproliferationandapoptosisofhumanhepatomacarcinomacells. Technol. Cancer Res. Treat. 2016, 15, 487–497.

[76] Pei, Z.; Zeng, J.; Gao, Y.; Li, F.; Li, W.; Zhou, H.; Yang, Y.; Wu, R.; Chen, Y.; Liu, J. Oxymatrine inhibits the proliferation of CaSki cells via downregulating HPV16 E7 expression. Oncol. Rep. 2016, 36, 291–298.

[77] Ye, J.; Zou, M.M.; Li, P.; Lin, X.J.; Jiang, Q.W.; Yang, Y.; Huang, J.R.; Yuan, M.L.; Xing, Z.H.; Wei, M.N.; et al. Oxymatrine and cisplatin synergistically enhance the anti-tumorimmunityofCD8+Tcellsinnon-smallcelllungcancer. Front. Oncol. 2018, 8, 631.

[78] Zhang, L.; Khoo, C.; Koyyalamudi, S. R.; Pedro, N. D.; Reddy, N. Antioxidant, anti-inflammatory, and anticancer activities of ethanol-soluble organics from water extracts of selected medicinal herbs and their relation with flavonoid and phenolic contents. Pharmacologia 2017, 8, 59–72.

[79] Behbahani, M.; Abolhasani, J.; Amini, M. M.; Sadeghi, O.; Omidi, F.; Bagheri, A.; Salarian, M. Application of mercapto-ordered carbohydrate-derivedporouscarbonsfortracedetectionofcadmiumandcopperionsinagriculturalproducts. FoodChem. 2015, 173, 1207–1212.

[80] Fiedor, J.; Burda, K. Potential role of carotenoids as antioxidants in human health and disease. Nutrients2014,6,466–488.