Review on Some Bangladeshi Medicinal Plants with Anticancer Properties

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(Received: June 13, 2021; Accepted: January 27, 2022; Published (Web): June 22, 2022)

ABSTRACT: According to WHO, cancer is one of the leading causes of death worldwide, accounting for an estimated 9.6 million deaths in 2018. More significant improvements have been made in the management and treatment of cancer, still there remains scope for the betterment of treatment procedures. Mostsynthetic anticancer drugs are known to develop resistance, show cytotoxicity against normal cells due to their non-selective nature, and cause tremendous side effects. Medicinal plants are significantly feasible sources of organic compounds, for their better availability, cheaper price, fewer side effects, and sometimes better therapeutic efficacy, which may benefit the world commercially or act as an important starting point for identifying lead compounds to develop modified derivatives. This article describes the ethnobotanical properties of 15 available medicinal plants of Bangladesh having anti-cancer properties.

Key words: Cancer, anticancer, medicinal plants, cytotoxicity.

INTRODUCTION

Multicellularity provides the great advantage of cell specialization, but the separate control of the proliferation of various specialized cell types is necessary. The cell cycle is shut down by terminal differentiation into the mature phenotype, whereas the arrest of progress in differentiation causes uncontrolled cell proliferation.[1] To avoid the growth or shrinkage of tissues, the rate of cell division must be equal to the rate of cell death in adult tissue. Normal cells only proliferate when developmental or other mitogenic signals in response to tissue growth requirements compel to do so.[2] If mutation to regulatory genes or other factors alters the normal cell cycle controls, the cells become vulnerable to deranged proliferation, which is the main hallmark of cancer.[3] According to WHO, the number of new cancer cases will be 15 million until 2020.[4] Medicinal herbs and their secondary metabolites are increasingly recognized as beneficial complementary treatments for cancer.[5]

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Dhaka Univ. J. Pharm. Sci. **21**(1): 95-104, 2022 (June)
DOI: https://doi.org/10.3329/dujps.v21i1.60401

Cancer chemotherapy causes significant side effects such as anemia, immunosuppression, hair loss, emesis, bruising, and bleeding. Though cytotoxic drugs target the proliferating cancer cells, but may also affect rapidly growing cells of the intestine, bone marrow, skin, and hair.[6] The mechanism of action of each chemotherapeutic agents is different, and different anticancer drugs work in other ways as the disease occurs due to random genetic mutations in various cell types.[7,8] Chemotherapeutic agents may become resistant to some normal cells due to dose-limiting toxicity.[9] Multidrug resistance may also occur in case of single cytotoxic agent exposure that may cause cross-resistance to other anti-cancer agents.[10] Again, surgery and first-line chemotherapy or radiotherapy can't remove every cancer cell, and these cells may cause clinical relapse later.[11] So, immune pharmacological studies aim to achieve a new treatment to improve cancer prognosis.[12]

Plant, herbal complexes, herbal products, or even a combination of plants are herbal drugs.[13] Herbal drugs are used to improve the disease, prevent metastasis, boost the immune system, release stress, and ensure relaxation.[14] They have been used to

avoid side effects occurring from using common treatment procedure that is chemotherapy or radiotherapy.[4]

The reviewdescribes the ethnopharmacological properties of available plants in Bangladesh, which may be potential candidates for cancer treatment.

METHODS

A literature survey was conducted ononline databases including Google Scholar, CAS, Science Direct and PubMed. Besides, manual searches were carried out in books and journals. For this review, all the data have been systematically compiled following the rigorous collection of information from the available sources.

Selected Plants and Their Chemical Constituents

Alstonia scholaris: Acubins/iridoids, saponins, phlobatanins, reducing sugars.[15] Fourpicrinine-type monoterpenoidindole alkaloids, 5-methoxyaspidophylline, picrinine (**1**), picralinal and 5-methoxystrictamine (**2**) were obtained from the leaves.[16]

Argemone mexicana: The flower contains tannins, saponins, glycosides, lignin, and phenol.[17] Protopine (**4**), berberine (**3**), dehydrocheilanthifoline, dehydrocorydalmine, jatrorrhizine, columbamine, (+)-reticuline, argemexicana A, argemexicana B, argemexinine, dehydrocoptisine, pancorine.[18]

Asclepia scurassavica: The cardenolides included calactin, calotropin, calotropagenin, coroglaucigenin, asclepin (**5**), asclepain CI, asclepain CII, uscharidin, uzarin, uzarigenin, corotoxigenin, asclepogenin, curassavogenin, calotroposide, clepogenin, desglucouzarin, kidjolanin (**6**), and uscharidin.[19]

Boerhavia diffusa: Root part contains punarnavoside, borhaavone, trans-caftaric acid, boeravinones (A-J, M, P-S) (**7**), 9-*O*-Methyl-10-hydroxy coccineone E, diffusarotenoid, 6-*O*-Demethyl-boeravinone H, 10-Demethyl boeravinone C, Coccineones E, B, boerhavine, liriodendrin, quercetine (**8**), syringaresinol mono-*β*-D-glucoside, hypoxanthine-9-L-arabinofuranoside, boerhavisterol, boeravilanostenyl benzoate, *β*-Ecdysone, triacont-24-en-1-oic acid, boeradiffusene.[20]

Carica papaya: Lycopene, ferulic acid (**9**), protocatechuic acid, *β*-carotene, chlorogenic acid, caffeic acid (**11**), *β*-cryptoxanthin, *p*-coumaric acid (**10**).[21]

Coix lacryma-jobi: Flavonoids, caffeic acid (**11**), ferulic acid, palmitic, stearic, oleic and linoleic acids, *β*-sitosterol, stigmasterol, vitamin E, squalene, campesterol (**12**).[22]

Cuscuta reflexa: Two known compounds such as 2-Methoxy-4-vinyl phenol and benzofuran-2,3-dihydro and other 12 unknown compounds such as 3,5-di-tert-Butyl-4-hydroxyanisole; hexatriacontane; n-hexadecanoic acid; scoparone; hexadecanoic acid methyl ester; 1,3-benzenediamine, *N*, *N*, *N′*, *N′* tetramethyl- have been isolated from the stem.[23] Phenolic compounds, hydroxycinnamic acid (**13**), phenylpropanoids, caffeic acid (**11**), kaempferol (**14**).[24] Reflexin, lutein, Lycopene, carotene, *α*-cryptoxanthin, amarbelin (pigment), phytosterols (seeds), abscisic acid (leaves), quercetin (**8**), cuscutin (stem), amino acids, cuscutalin, caffeic acid etc.[25]

Colocasia esculenta: Leaves contain calcium oxalate, fibers, minerals (calcium phosphorus, etc.), and starch, vitamin A, B, C, etc. From the tubers, two dihydroxysterols, 14α-methyl-5α-cholesta-9, 24-diene-3b, 7α-diol and 14α-methyl-24-methylene-5α-cholesta-9, 24-diene-3α, 7α-diol, anthocyanine (**15**), luteoline (**16**), besides *β*-sitosterol and stigmasterol, nonacosane and cyanidin 3-glucoside.[26]

Celosia argentea: Alkaloids, saponins, cardenolide and dienolides, phenolics, flavonoids.[27] Eight saponinscelosin A, celosin B, celosin C, celosin D, celosin E (**18**), celosin F (**17**), celosin G and cristatain. Two novel saponinscelosin I and celosin II were isolated from the 50% EtOH extract.[28]

Ficus racemose: Leucocyanidin (**19**), leucocyanidin-3-*O*-*β*-D-glucopyrancoside, leucopelargonidin-3-*O*-*β*-D-glucopyranoside, leucopelargonidin-3-*O*-*α*-L-rhamnopyranoside.[29]

Fruit contains glauanol, hentriacontane, glauanol acetate, glucose, tiglic acid (**20**), esters of taraxasterol, lupeol acetate, friedelin, higher

hydrocarbons.[30] A new tetra triterpeneglauanol acetate- 13*α*, 14*β*, 17*β*H, 20 α H-lanosta-8, 22-diene-3*β* acetate and racemosic acid.[31]

Hyptis suaveolens: The terpene alcohol eucalyptol (**21**), gama-ellemene (**22**), beta-pynene, (+)3-carene, trans-beta-cariophyllene and germacrene.[32] 1, 8-cineole and *β*-caryophyllene, *α*-pienene, camphene, sabinene, *β*-pinene, myrcene, α-phellandrene, *γ*-terpinene, *α*-terpinolene, linalool, fenchol, 4-terpinenol.[33]

Ipomoea quamoclit: Seeds contain lauric acid (**23**), resin glycosides, quamoclins I-IV and jalapin, 7-*O*-*β*-D-glucopyranosyl-dihydroquercentin-3-*O*-*α*-D Glucopyranosi.[34] Pyrrolizidine alkaloids like mono and diesters of platynecine and minalobines like minalobine O and R, ipangulines like ipangualine B2 (**24**) and D11 and ergoline alkaloids and anthocyanins.[35]

Justicia adhatoda: A bitter quinazoline alkaloid, vasicine(**25**), vasicinone (**26**) has been isolated from the plant's leaves, roots, and flowers (0.0541 to 1.105%).[36] Deoxyvasicinone, 7-methoxyvasicinone, desmethoxyaniflorine, 3-hydroxyanisotine, vasnetine.[37]

Trichosanthes anguina: Ascorbic Acid, *β*-carotene, riboflavin (**27**), thiamine (**28**), stearic acid, sulfur.[38]

Xanthium strumarium: Proteins, carbohydrates, phenols, tannins, flavonoids, saponins.[39] Chlorogenic acid, cynarin, 1, 5-*O*-dicaffeoylquinic acid; 1, 4-*O*-dicaffeoylquinic acid; 1, 3, 5-*O*-tricaffeoylquinic acid and 3 heterocyclics.[40] 7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzol [1,4] thiazine-3,5-dione-11-*O*-*β*-D-glucopyranoside and 2-hydroxy-7-hydroxymethyl-8,8-dimethyl-4,8-dihydrobenzol [1,4] thiazine-3,5-dione-11-*O*-*β*-D-glucopyranoside.[41] Xanthumin (**29**), formononetin (**30**), xanthatin (deacetylxanthinin), xanthostrumarin, atractyloside, carboxyatractyloside, phytosterols, xanthanol, isoxanthanol, xanthinosin.[42]

Anticancer Properties of the Selected Plant Species

***Alstonia scholaris* (Apocynaceae):** The triterpenoids (lupeol linoleate, lupeol palmitate, alpha-amyrin linoleate) acted by inhibition of tumor invasion, metastasis, and angiogenesis.[43] Ethanolic extract worked in combination with berberine hydrochloride,a topoisomerase inhibitor.[44] Ethanolic extract acted on human neoplastic cell lines like HeLa, KB, HepG2, MCF-7, and HL60.[45] Aqueous extract had the anticancer effectin 7, 12 dimethylbenz (a) anthracene C (DMBA) induced skin cancer.[46]

***Argemone Mexicana* (Papaveraceae):** Alkaloids isolated from the plant worked against human nasopharyngeal carcinoma (HONE-1) and human gastric cancer (NUGC) cell lines.[47] Ethanolic extract showed an anticancer effect on cancer cell lines of HeLa-B75, HL-60, and PN-15 cancer cells.[48] Methanolic extractinhibited the growth of the HeLa and MCF-7 cells.[49]

***Asclepia scurassavica* (Asclepiadaceae):** *β*-sitosterol showed anticancer effect by inhibition of COLO 320 DM cells, induction of apoptosis, and suppression of the expression of β-catenin and PCNA in human colon cancer cells.[50] Calotropin acted against human carcinoma of the nasopharynx.[51,52] Methanolic extract showed effect against Hep-2 cell line.[53] Cardenolides worked against human lung carcinoma A549, two human breast carcinomas MCF-7 and MDA-MB-231and hepatoma HepG2.[54] Dioxane double-linked cardenolide glycosides and cardenolide lactates acted against DU145 prostate cancer cells.[55] Asclepiasterol worked by reversing Multi-Drug Resistance (MDR) intervened by P-glycoprotein (P-gp).[56]

***Boerhavia diffusa* (Nyctaginaceae):**Root extract showedeffect in HeLa and U-87 tumor cell lines.[20] 95% ethanolic extract had an anticancer effect on lymphoma and leukemic cells.[57] Boeravinones G (1) and H (2)had inhibiting effect on breast cancer resistance protein (BCRP/ABCG2).[58] 95% ethanolic extract of the root portion workedon the HeLa cell line.[59] The methanolic extract showed an effecton the MCF-7 cell line and reduced the viability of cells.[61]

Methanolic extractinhibited theB16F10 melanoma cells.[61] Punarnavine showed anticancer effectby increasing NK cell activity.[62]

***Carica papaya* (Caricaceae):** Lycopenehad effect on the liver cancer cell line Hep G2.[63] Seed extract worked on leukemia HL-60 cells.[22] Ethanolic extract inhibited the growth of cancer cells.[64] *C. papaya* contains ribosome-inactivating proteins which has shown cytotoxicity against breast cancer cell line, T47D.[65] Aqueous extract acted against stomach cancer cell line (ags), pancreatic cancer cell line (capan-1), colon cancer cell line (dld-1), ovarian cancer cell line (dov-13), lymphoma cell line (karpas), breast cancer cell line (mcf-7), neuroblastoma cell line (t98g), uterine cancer cell line (hela).[66] Aqueous extract had effect on breast cancer cell line (MCF-7).[67] n-Hexane extract worked on leukemia HL-60 cells.[68] Fabricated high-stable silver nanoparticles (CPAgNPs) prepared using *C. papaya* had an anticancer effect on MCF-7 cells.[69] Aqueous extract worked on tumor cell lines and human peripheral blood mononuclear cells (PBMC).[70] Papain isolated from the plant showed an anticancer effect by breaking down that fibrin coat of cancer cell wall.[71]

***Coix lacryma-jobi* (Poaceae)**:Methanolic extract acted on A549 lung cancer cells.[72] Trans-coniferylaldehyde isolated from the plant is a potent chemopreventive agent.[73] A triterpene-loaded microemulsions (TMEs) called Ganoderma lucidum was prepared using seed oil acted against human lung carcinoma (A549) cells and murine lung tumor (Lewis) cells.[74] Seed extract worked on HCC cell line HepG2 cells.[75] Four free fatty acids: palmitic, stearic, oleic, and linoleic acids were found to possess antitumor activity.[76]

***Cuscuta reflexa* (Cuscutaceae)**: Chloroform and ethanol extracts acted against Ehrlich Ascites Carcinoma (EAC) cell line.[77] *Cuscutareflexa* has shown anticancer activity against leukemias and melanoma.[78] It has also shown anticancer activity on Hep3B cells by up-regulation of pro-apoptotic factors BAX and p53and downregulation of anti-apoptotic factors Bcl-2 and surviving.[79] Natural products isolated worked on HCT116 colorectal cancer cell line.[80] Methanolic extracthave shown cytotoxicity in Brine Shrimp lethality assay, may be due to the presence of phenols, polyphenols, and flavonoids.[81]

***Colocasia esculenta* (Araceae)**: Plant extract had effect on colon cancer.[82] Water-soluble extracts showed effect in a murine model of highly metastatic ER, PR and Her-2/neu negative breast cancer.[83] Taro-4-Iisolated actedby increasing the production of interleukin (IL)-6 and tumor necrosis factor-α (TNF-α).[84] A mitogenic lectin called Tarin isolated from this plant showed noteworthy anti-tumor activities.[85]

***Celosia argentea* (Amaranthaceae)**: Celosianinduced tumor necrosis factor-α (TNF-α) production and gamma interferon (IFN-y) production activity of concanavalin A (Con A) in mice spleen cells.[86] Three new triterpenoidsaponins-celosin E, celosin F and celosin G with cristatain showed antitumor activity.[87] Seed extract acted on colon 26-L5 carcinoma cells.[88] A novel anticancer phenolic compound; (1-(4-hydroxy-2-methoxybenzofuran-5-yl)-3-phenylpropane-1, 3- dione) has been isolated from the plant.[89] Stigmasterol had effect against human gastric cancer cells SGC-7901 and human hepatoma cells BEL-7404.[90]

***Ficus racemose* (Moraceae)**: Methanolic extract showed effect on KBrO3-mediated nephrotoxicity.[91] Ethanolic fruit extract worked on MCF7 human breast cancer cells.[92] Plant extracts acted against lung carcinoma cell line Calu6.[93] Methanolic extract had an anticancer effect against HL-60 and HepG2 cell line.[94]

***Hyptis suaveolens* (Lamiaceae):** The leaves are used as anticancer remedy.[32] Essential oil of the leaves acted on the human breast cancer cell line (MCF-7).[95] Ethanolic extracthas increased hemoglobin, RBC, and WBC in tumor-bearing mice.[96]

***Ipomoea quamoclit* (Convolvulaceae):**Ethanolic extract worked by inhibiting Caco-2 (colon cancer) cell viability.[97] Dichloromethane, methanol, hexane and ethyl acetate extracts of leaves had anticancer effect on HeLa, MCF-7, CNE-1, 3T3 and HT-29 cell

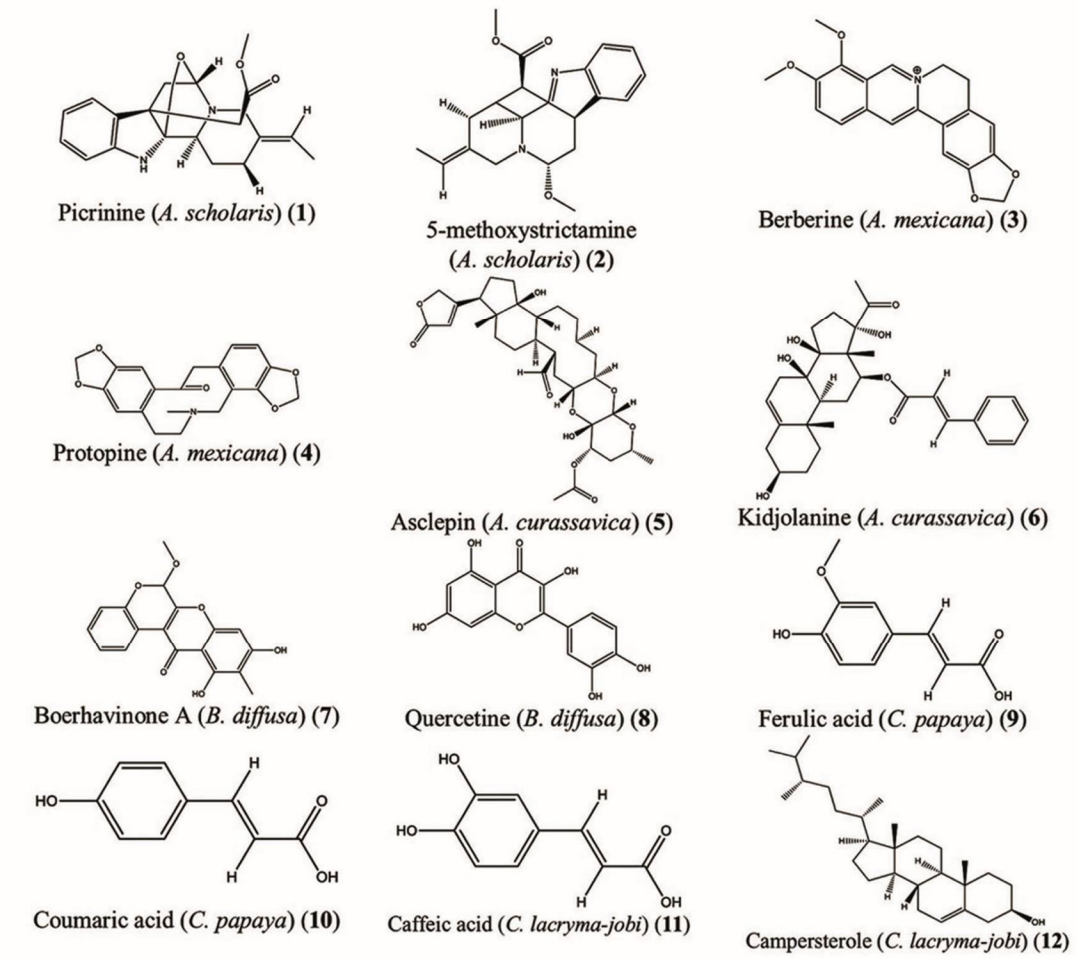
lines.[98] Aqueous leaves extracts worked on HEP G2 cell line byinhibiting A549 cell line.[99]

***Justicia adhatoda* (Acanthaceae):** Methanolic extractinhibited the proliferation of theMCF-7 cell line.[100] 80% ethanolic extract showed a possible chemopreventive role.[101] Vasicine acetate, obtained by acetylation of vasicineisolated, showed effect on A549 lung adenocarcinoma cell line.[102]

***Trichosanthes anguina* (Cucurbitaceae):** A study has shown that *Trichosanthesanguina* contain a type I ribosome-inactivating protein (RIP), named trichoanguin has a great potential to be used as a chemotherapeutic agent to treat cancer as it strongly inhibits the protein synthesis of rabbit reticulocyte lysate but only weakly that of HeLa cells.[103]

***Xanthium strumarium* (Asteraceae):** 8-epi-xanthatin and 8-epi-xanthatin epoxide acted on human A549, SK-OV-3 (ovary), SK-MEL-2 (melanoma), XF498 (central nervous system) and HCT-15 (colon) cell in vitro.[104] Plant extractshowed inhibitory effect on three human cell lines (breast MCF7, renal TK10 and melanoma UACC62).[105] Xanthatin and xanthinosin, 2 sesquiterpene lactones had effect on human cancer cell lines WiDr ATCC (colon), MDA-MB-231 ATCC (breast), and NCI-417 (lung).[106] Methanolic extract acted on HeLa cell line.[107] Methanol extracts worked against HepG2, A549, L929 and Jurkat cell lines.[108] It has shown anticancer activity in a study in murine tumor model.[109] Methanolic extract had shown anticancer effect against Dalton's ascitic lymphoma (DLA) induced solid and liquid (ascites) tumor in mice.[110]

The structures of some of the constituents isolated from the discussed plants are demonstrated in Figure **1**.



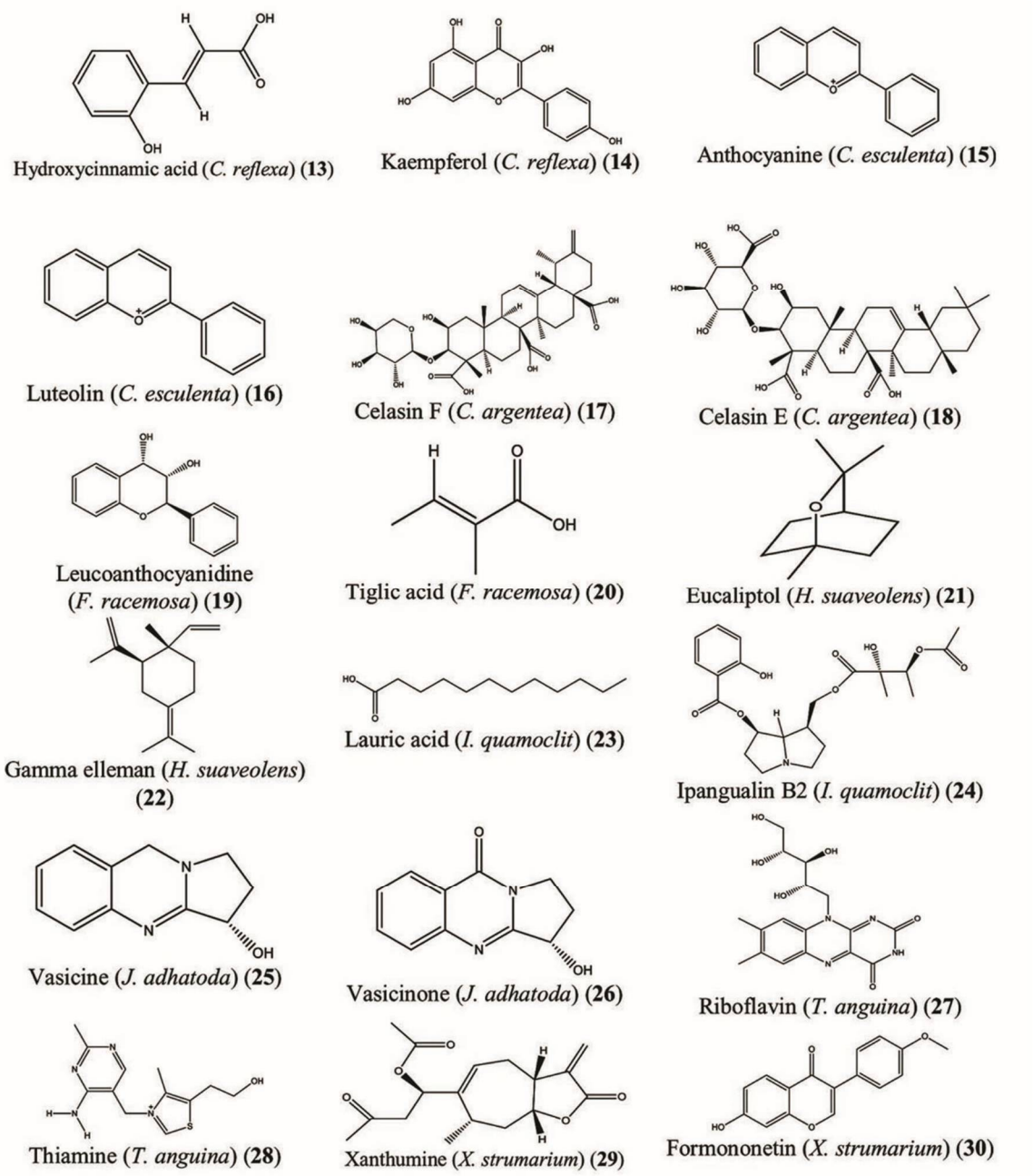


Fig. 1. Structures of some isolated constituents from fifteen (15) Bangladeshi medicinal plants.

DISCUSSION

It has been reported that about 80-85% population all over the world are dependent on herbal medicine as their first-line treatment procedure of any disease and major part of treatment with medicinal plants involves the exploitation of plant extract and their active constituents. A lot of clinical studies have proved the positive outcome of herbal medicines on the survival, immunomodulation and quality of life of cancer patients when they are used along with conventional therapy. There are some plant-derived compounds which have definite anticancer properties approved by USFDA such as taxol, taxotere, vincristine, navelbine, etoposide, teniposide,

topotecan and irinotecan. A more extensive search should be carried out to find out the unexplored plants which may have anticancer properties.

CONCLUSION

The use of medicinal plants in the management and treatment of carcinogenic progression provides an alternative solution to the use of synthetic allopathic anticancer medication. The most vital target of cancer treatment is to destroy cancer cells in the presence of normal cells without damaging them. So, investigation of cytotoxic compounds and crude extracts of plants are necessary to develop alternative treatment procedure of cancer. Medicinal plants are attracting worldwide attention for their feasibility. For its cheaper price, initiatives may be taken to introduce herbal products in the rural areas of Bangladesh in the treatment of cancer. Proper management and cultivation are required to preserve these plants to study them in the future.

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