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Bioactive Properties of Momordica Charantia as Anti-Cancer/ Anti- Neoplastic Agent

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ABSTRACT:-
Momordica charantia L., a plant native to tropical and subtropical regions, has been used in folk medicine for treating diabetes mellitus and as a vegetable for thousands of years. It contains phytochemicals such as proteins, polysaccharides, flavonoids, triterpenes, saponins, ascorbic acid, and steroids. M. charantia has various biological activities, including antihyperglycemic, antibacterial, antiviral, antitumor, immunomodulation, antioxidant, antidiabetic, anthelmintic, antimutagenic, antiulcer, antilipolytic, antifertility, hepatoprotective, anticancer, and anti-inflammatory activities. However, it has also been found to exert toxic or adverse effects under different conditions.
Momordica charantia is known for its functional food properties, which prevent and treat diabetes mellitus and associated complications, as well as cancers. Recent research using modern techniques has revealed the anti-cancer activities of M. charantia, a plant with significant health benefits. Researchers have found that M. charantia-related extracts and compounds have been successful in treating cancer cell lines by inducing cell cycle arrest and apoptosis without affecting normal healthy cell growth. This review highlights recent advancements in the anti-cancer effectiveness and chemopreventive ability of M. charantia and its active constituents, with a focus on cucurbitane-type glycosides, ribosome-inactivating inhibitors, and conjugated fatty acids.
KEYWORDS:- Cucurbitaceae family, adverse effect, diabetes mellitus,brain cancer,Momordica charantia,biological activities,subtropical region.

I. INTRODUCTION:-

Cancer is a leading cause of death worldwide, accounting for millions of deaths each year[1]. Studies have shown that the intake of antioxidant-rich foods can prevent cancer, cardiovascular diseases, diabetes, and other chronic diseases.[2] The highly reactive and bioactive phytochemical antioxidants in plants are postulated to be responsible for the protective effects of plant foods. Biochemically active phytochemicals found in plant-based foods also have powerful biological properties that are not necessarily related to their antioxidant properties.[3][4] Some cancer patients use agents derived from different plants or nutrients as complementary or alternative medicines, exclusively or concurrently with traditional chemotherapy and/or radiotherapy.[5]The discovery of food plants with medicinal effects has prompted studies evaluating possible anticancer agents in fruits, vegetables, herbs, and spices. Momordica charantia L. (bitter gourd), a member of the Cucurbitaceae family, is widely grown in tropical areas and used as a traditional medicine plant indigenous to China. It has been found to possess antiviral, antibacterial, and immunomodulatory properties and is often used as a topical remedy for expelling intestinal gas and treating skin problems. In Taiwan, both cultivars and wild-grown M. charantia are found.[6]M. charantia contains an array of components with different biological activities. Extracts of the fruit of M.charantia were suggested to modulate signal transduction pathways for inhibition of breast cancer cell growth.In vitro studies suggest that alpha- and beta-mormorcharin exert possible anti-herpes-virus effects, while momordin, a protein found in M. charantia, has anticancer activity in animal experiments. MAP30, a 30-kDa protein isolated from seeds of M. charantia, has shown promising effects for treating tumors and HIV infection[7][8][9]

II. TRADITIONAL USES OF

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MOMORDICA CHARANTIA:-

Momordica charantia L., also known as bitter melon or bitter gourd, is a plant native to tropical and sub-tropical regions. Its fruits and leaves are rich in phytochemicals, offering health-promoting effects through nutritionaland nutraceutical components[10].The plant has been used in traditional and folk medicines for various medicalapplications, including treating T2DM, hypertension, obesity, cancer, bacterial and viral infections, and AIDS[11]. In Ayurveda medicine, bitter melon, known as karela, has been used for thousands of years due to its pharmacological properties. The juice of the plant is used for various disorders, such as joint pain relief, chronic fever, jaundice, liver and digestive system illnesses, and treating burns, boils, and rashes. The whole plant is recommended for treating T2DM[12]. In Turkish folk medicine, the oil obtained from the ripe fruits is combined with honey for gastric ulcer prevention and healing. In African folk medicine, bitter melon is used for worm infections, inflammation, fever, menorrhea, syphilis, rheumatism, and skin diseases. Leaf decoction is used in T2DM patients, while fruits and leaves are used for jaundice, liver diseases, ulcers, burns, gonorrhea, measles, chicken pox, scabies, and malaria. In the Caribbean, it is administered as a leaf decoction or fruit juice for diabetes treatment, high blood pressure, womb infections, malaria, dysentery, and worm infections.[13]

III. MECHANISM OF MOMORDICA CHARANTIA PHARMACOLOGICAL EFFECT:-

Momordica Charantia Molecular Mechanism Target Cancers

IV. THE ACTIVITY OF MOMORDICA CHARANTIA ON CANCER:-

Bitter melon extract and its active ingredients have been studied in laboratory and pre-clinical cancer models, but clinical studies are lacking. Preventive studies were conducted on various cancers, using crude extracts prepared from water, methanol, or ethanol. Therapeutic studies were conducted on various cancers in vitro and in vivo. The effect of bitter melon on cancer chemoprevention and therapy is summarized in Table 1, Figure 2, and discussed further.

V. MOMORDICA CARANTIA PREVENTIVE AND THERAPEUTIC EFFECTS OF VARIOUS CANCERS:-

Cancer Model	Momordica Charantia Extract/Compounds	Preventive and Therapeutic Effect	Reference

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Blood	Water etract of food,MAP30,Seed extract, and α-eleostearic acid	1. The growth of leukemia cells HL-60, THP-1, HL60 ED, Su9T01, HUT-102, and Jurkat was suppressed, leading to apoptosis. 2. Suppressed the development of tumors in mice, resulting in improved survival and enhanced immune function.	[14][15][16][17][18]
Brain	α, β momorcharin, 25-diene-3-O-β-d- glucopyranoside, MAP30, charantagenins D, E.	1. Glioma cells experienced suppressed growth, movement, and invasion, while also undergoing programmed cell death. 2. The proliferation, migration, and invasion of glioma cells were hindered, leading to an increase in apoptosis. 3. Glioma cell proliferation and migration were inhibited, along with a reduction in invasion, ultimately resulting in induced apoptosis.	[19][20][21][22]
Breast	25-trihydroxycucurbita- 5,23(E)-dien-19-al (TCD), eleostearic acid, RNase MC2, MAP30, Water extract of fruit, dried extract and isolated compounds 3β,7β.	1. The growth of breast cancer cells was suppressed, leading to both apoptosis and autophagy. 2. The development of syngenic tumor,	[23][22][24][25][26][27][28][29][30][31]

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		xenograft tumor, and spontaneous mammary tumorigenesis in SHN virgin mice was effectively inhibited.	
Colon	some isolated cucurbitane-type triterpene glycosides, seed oil, α-eleostearic acid, MAP30 and Methanol extract of fruit, seed extract.	1. The growth of colon cancer cells was suppressed, leading to a halt in the cell cycle, cell death, autophagy, increased sensitivity to doxorubicin, and inhibition of cancer stem cells. 2. The development of colon cancer caused by azoxymethane (AOM) was successfully prevented in F344 rats.	[23][16][22][32][33][34][35][36][37]
Head and neck	Water extract of fruit	1. Oral cancer cell growth, metabolism, and survival were suppressed, leading to programmed cell death in oral cancer cells. 2. Oral cancer syngenic tumor, xenograft tumor, and mouse tongue carcinogenesis induced by 4NQO were reversed, resulting in tumor regression.	[38][39][40][41][42]

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Kidney	Water extract	1. Adrenocortical cancer cell growth was suppressed, steroid production was inhibited, and apoptosis was triggered. 2. The proliferation of adrenocortical cancer cells was restrained, steroid hormone synthesis was suppressed, and programmed cell death was induced. 3. Suppression of adrenocortical cancer cell proliferation, inhibition of steroid hormone production, and initiation of apoptosis were observed.	[43]
Liver	MAP30, RNase MC2, lectin, Water extract of fruit, methanol extract and isolated compounds karaviloside III.		[44][45][46][47]
Lung	MAP30 and α-MMC, methanol extract of leaf, Water extract.	1. Human lung cancer cells experienced suppressed cell growth, movement, and invasion, while also undergoing cell cycle arrest and programmed cell death.	[48][49][50]
Ovary	Water extract of fruit and kuguacin J	1. Human ovarian cancer models, both in vitro and in vivo, exhibited suppressed growth, triggered cell death, and increased sensitivity to cisplatin treatment. 2. The growth of human ovarian cancer was hindered, apoptosis was induced, and the response to cisplatin was enhanced in both in vitro and in vivo models.	[51][52]

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		3. In both in vitro and in vivo models, human ovarian cancer demonstrated inhibited growth, apoptosis induction, and heightened sensitivity to cisplatin.	
Pancreas	Water extract of fruit	1. Cancer cell proliferation, metabolism, and xenograft tumor growth were effectively inhibited, leading to apoptosis induction. 2. The growth of cancer cells and xenograft tumors was	[53][54][55][56]
		suppressed, while metabolism was halted, ultimately resulting in apoptosis. 3. Inhibition of cancer cell proliferation, metabolism, and xenograft tumor growth was observed, accompanied by the induction of apoptosis.	
Prostate	30 kDa protein from seeds (MCP30), leaf extract, kuguacin J, Water extract of fruit.	1. Prostate cancer cells experienced suppressed cell growth, cell division, and spread. 2. The development of xenograft tumors and spontaneous tumors in TRAMP mice was effectively halted.	[57][58][59][60]

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Skin	Cucurbitane-type triterpenes compounds from fruit, Water extract of fruit, methanol extract of fruit and leaf.	1. Mice were protected against melanoma syngeneic tumor growth and skin carcinogenesis induced by DMBA/croton oil or DMBA/peroxynitrite.	[61][62][63]
Stomach	Fruit extract, methanol extract of leaf and fractioned proteins I–III	1. Human gastric cancer cell lines exhibited significant anti-cancer effects when tested. 2. The development of forestomach papillomagenesis in mice induced by benzo(a)pyrene [B(a)P] was effectively prevented.	[64][65][66]
Uterine cervix	Leaf extract and kuguacin J	1. The human cervical carcinoma cell line (KB-V1) showed reduced resistance to vinblastine and paclitaxel. 2. Vinblastine and paclitaxel resistance was overcome in the human cervical carcinoma cell line (KB-V1). 3. The KB-V1 cell line exhibited suppressed resistance to vinblastine and paclitaxel in human cervical carcinoma.	[67]

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M. charantia is a plant that has been used to prevent childbirth in India[68], with its ethanolic extract having a greater impact on spermatogenesis and causing histological changes in testis and accessory reproductive organs of albino mice[69]. In female Wistar rats, aqueous leaf extracts decreased plasma progesterone and estrogen levels in a dose-dependent manner compared to the controls[70]. RIPs were also found to have antifertility activity[71]. α-MMC could induce termination of early pregnancy and cause abortion, possibly due to the inhibition of morulae development[72].Subcutaneous injection of alcoholic extracts mainly induced acute symptoms such as changes in respiratory and heart rates, leading to pathological changes in these organs. M. charantia juice showed a much stronger effect with a LC50 = 91.9 mg/100 g body weight (b.wt.), compared to alcoholic extracts of 362.34 mg/100 g b.wt[73]. Clinical studies have shown that high-dose ingestion of M. charantia fruit causes abdominal pain and diarrhea in diabetes[74]. The aqueous extract was reported to significantly decrease hemoglobin concentration of albino rats[75]. M. charantia lectin had a cytotoxic effect, inhibiting DNA and protein synthesis in human peripheral blood lymphocytes[76].

VI. CHEMICAL COMPOSITION:-

M. charantia fruit contains various bioactive compounds, including carbohydrates, proteins,lipids[77][78][79], triterpenoids[80][81][82][83], saponins[84][85][86], polypeptides[87], flavonoids[88], alkaloids[89], and sterols[82], as recorded in literature. Previous phytochemical studies have demonstrated the bioactive components and their related functions, as shown in Table 2.

Major Bioactive Components	**Functions**	**Distribution**	**Reference**
Polysaccharides	Neuroprotective, antitumor, antioxidant, antidiabetic, immune enhancement.	Various parts of plants	[90][91][91][93][94][95]
Peptides and proteins	DNase-like, phospholipase, superoxide dismutase,anti-tumour, RNA N-glycosidase, polynucleotide adenosine glycosidase (PAG), anti- tumour, immune suppression, antimicrobial.	Seed	[96][97][98][99][100][101][102]
Lipids	Antitumor, antioxidant	Seed, flesh	[103][104][105]
Terpenoids	hypoglycemic, cancer chemoprevention, Anticancer, antioxidant, antidiabetic.	Stem, leave, fruit	[106][107][108]
Saponins	antihyperglycemic, hypolipidmic, antiviral.	Fruit, root, seed	[109][110][111][112][113][114] [115][116]
Phenolics	Antioxidant, anti-inflammation, immune enhancement	Fruit, pericarp, seed	[117][118][119][120]

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6.1.POLYSACCHARIDES:-

Polysaccharides are crucial bioactive components of M. charantia fruits, with various bioactivities including antioxidant, antidiabetic, immune-enhancing, neuroprotective, antitumor, and antimicrobial properties. They make up about 6% of bitter gourd powder and are classified as heteropolysaccharides. Polysaccharides can be influenced by various conditions and are classified into two main fractions. Acidic and branched heteropolysaccharides (MCBP) and pectic polysaccharides have antioxidant, α-amylase, and angiotensin- converting enzyme functions[121]. A water-soluble polysaccharide (MBP) was isolated from M. charantia fruits and showed a significant hypoglycemic effect. M. charantia polysaccharides can ameliorate oxidative stress, hyperlipidemia, inflammation, and apoptosis during myocardial infarction by inhibiting the NF-κB signaling pathway.[122][123][124]

6.2.PROTEINS AND PEPTIDES:-

M. charantia fruit and seeds contain various proteins and peptides, including ribosome inactivating proteins (RIPs), Momordica charantia lectin (MCL), Momordica anti-HIV protein of 30 kD (MAP30), α-momorcharin (α- MMC), β-momorcharin, γ-momorcharin, δ-momorcharin, and ε-momorcharin. These proteins possess various activities, including RNA N-glycosidase, PAG, DNase-like, phospholipase, superoxide dismutase, anti-tumor, anticancer, immunosuppressive, and anti-microbial properties. RIPs are RNA glycosylases that inhibit protein synthesis by inactivating ribosomes. M. charantia lectin and α-MMC have been isolated from M. charantia seeds, which can inhibit human nasopharyngeal cancer cells and xenograft tumors in vitro. MAP30, a single- chain RIP, has strong anti-tumor potential and inhibits proliferation in various cancer cells. Polypeptide-P, a hypoglycemic peptide, is also found in M. charantia fruit, seeds, and tissues. Other proteins and peptides have also been isolated from M. charantia[90][91][91][93][94][95].

6.3.SAPONINS AND TERPENOIDs:-

Saponins are glycosides found in M. charantia, found in its roots, stems, leaves, and fruit. They are primarily composed of tetracyclic triterpenoids and their glycosides, known as cucurbitanes, which are known for their bitterness and toxicity. M. charantia contains triterpenoidal saponins and steroidal saponins, which are used in various drugs. Cucurbitanes from M. charantia are responsible for their anti-diabetic and hypoglycaemia activities. Studies have isolated various compounds from M. charantia, including goyaglycosides, goyasaponins, momordicosides, and kuguaglycosides. Additionally, new cucurbitane-type triterpenoids have been isolated from M. charantia stems and rattans.[125][126][127]

6.4.FLAVONOIDS AND PHENOLIC COMPOUNDs:-

M.charantia contains various flavonoids and phenolic compounds, including gallic acid, protocatechuic acid, gentistic acid, (+)-catechin, vanillic acid, syringic acid, (−)-epicatchin, p-coumaric acid, benzoic acid, sinapinic acid, o-coumaric acid, chlorogenic acid, t-cinnamic acid, and t-ferulic acid[128]. The most abundant flavonoids are quinic acid and catechin. Phenolic acid constituents vary among tissues. The main phenolic acids in bitter melon flesh are gallic acid, gentisic acid, catechin, chlorogenic acid, and epicatechin[129]. Catachin and epicatechin are the most common flavonoids in plants. Caffeic acid is classified as a phenylpropanoid and is found in the methanolic fraction.

6.5.OTHER COMPONENTs:-

M. charantia contains bioactive ingredients, unsaturated fatty acids, alkaloids, amino acids, minerals, and vitamins[130][131][132]. The proportion of unsaturated fatty acids is high, with monounsaturated fatty acids at 20.1% and polyunsaturated fatty acids at 64.3%. Nine types of unsaturated fatty acids are found in bitter melon extracts. M. charantia is also a natural source of vitamins, including ascorbic acid.

VII. CONCLUSION:-

Momordica charantia, a tropical plant, has antiviral, antibacterial, and immunomodulatory properties. It has been used in traditional and folk medicines for various medical applications, including treating T2DM, hypertension, obesity, cancer, bacterial and viral infections, and AIDS. Recent research using modern techniques has revealed the anti-cancer activities of M. charantia, with extracts and compounds successfully treating cancer cell lines by inducing cell cycle arrest and apoptosis without affecting normal healthy cell growth.

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Research on the bioactivities of M. charantia has rapidly developed, with the separation and identification of bioactive components attracting more attention. Clinical studies should focus on the components, especially polysaccharides, to clarify the relationship between structure and mechanisms of efficacy.

Potential adverse effects should be investigated further, including potential side-effects on the human body, hypoglycemia in diabetic patients, and the need for special populations to follow doctor or expert recommendations. Most existing studies on bioactive components are performed at the animal and cell levels, so clinical research is needed before their application in relevant industries.

M.charantia application in food and pharmaceutical fields is still in the initial processing stages, and its health benefits are not yet fully utilized.

ABBREVIATION:-

MAP30	Momordica anti-HIV protein
30-kDa	30-kilodalton
T2DM	Type 2 diabetes mellitus
AIDS	Acquired Immune Deficiency Syndrome
HL-60	human leukemia cell line-60
THP-1	Human leukemia monocytic cell line
HL60 ED	Human promyelocytic leukemia cell line-60
AOM	Azoxymethane (AOM)
α-MMC	Alpha-momorcharin

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