A BRIEF REVIEW ABOUT THE NATURAL PRODUCTS IN CANCER THERAPY WITH THEIR MECHANISM OF ACTION AND THEIR TOXICITY FROM THE PAST DECADES

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Abstract

Cancer is a major world public health problem, associated with chemotherapy treatments whose administration leads to other secondary problems. Oral cancer is one of the usual causes of mortality in world, with a five year survival rate of only 50%. The OC is generally treated primarily by surgery with or without adjuvant radiotherapy / or chemotherapy. But these therapy and treatments are generally shows major side effects like loss of hairs, loss of appetite, neurons functional loss etc. Nowadays natural products are leading candidates in treatment of oral cancer. There is a number of dietary supplements like fruits and vegetables that are rich in phytochemicals and provides a variety of antioxidants like vitamin A,C,E, Curcumin, NEEM, Green Tea, some medicinal Mushrooms. This article gives you a brief knowledge about how natural products can act in fighting against oral cancer and prevent oral cancer by less toxic effects and higher efficacy.

Key points: Oral Cancer, Cancer profile, Risk Factors, Treatment options for cancer, Natural products as chemoprventive agents, Antioxidants in oral cancer, Yoga in OC, SWOT Analysis.

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1. Introduction

Oral Cancer

Oral cancer is one of the most widest and deadliest of disease all over the world with a 5 year survival rate of 50% only. [1, 2] Annually an estimated 400,000 people worldwide are newly diagnosed with oral cancer particularly high among men. According to a study of world health report, published in 2005, the frequency rates for oral cancer oral cancer differ in man from 1 to 10 cases per a population of 100,000 in most of countries. The rate of oral cancer in India is 12.6 per a population of 100,000. Females are less affected (20.5%) in Compare to male (48.2%). 30-35% of Indian population is affected with oral cancer. [1,3]

Oral cancer is a highly relevant problem of global public health, especially for dental surgeons. OC is located in top 10 ranking incidence of cancer & despite the progress in research and therapy, survival has not improved significantly in the last years, representing a continuting challenge for biomedical sciences. [4]

Oral squamous cell carcinoma (OSCC) is one of the most prevalent oral cancer, the risk of which is increasing in individuals under 40years old, particularly in developed countries. [5]

The understanding of data from epidemiological studies is sometimes difficult to read into. The term "oral cancer", in some reports included all malignancies arising from the lips, oral cavity, oropharynx, nasopharynx, & hypopharynx, whereas other descriptions include we just intraoral sites and pharynx. Head and neck cancer include cancers of oral cavity, pharynx & larynx. It is been documented of that oral and pharyngeal cancer together where the sixth most common cancers in the world. [6,7]

Cancer Profile

Oral cancer constitutes 15% to 20% of all cases seen in various cancer hospitals in India. In an effort to characterize the demographic features of patients with oral cancer, we described the clinical profile of 2007 patients with oral cancer to another article. [8,9]

The peak age frequency distribution was seen in the sixth decade for men and in seventh decade for women.74% of patients had cervical lymph node involvement at the time of their initial visit. Only 12% had localized cancers. Data from the major cancer hospitals in India indicate that 60% to 80% of patients also had lymph node involvement at the time of presentation and only 10% - 15% had "localized" (T1 , T2) cancer. [10]

Moreover, in a large no. of patients extensive soft tissue and bone involvement makes a primary surgical approach elaborate & mutilating. A wide number of competing illnesses requiring emergency and elective surgical interference make oral cancer a lesser priority in many general surgical departments. [11]

Risk Factors

The most significant risk factor for the development of oral cancer in the western countries for the consumption of tobacco [12] & alcohol [13]. Although drinking and smoking are independent risk factors, they shows synergistic effect and greatly increase risk together. In Asian countries, the use of smokeless tobacco products such as guthka, pan masala, betel quid [14,15] is responsible for a considerable percentage of oral cancer cases. [16]

The familial risk for oral cancer could be acquired as result of imitating high risk habits within the family, such as smoking and drinking or as genetic trait. [17]

Treatment

Conventional treatment (CT) for OC include chemotherapy, radiotherapy, and mainstay surgery (depending on the tumor location & stage) & are focused on eradicating the tumor mass. Despite the benefits, these treatments have associated side effects, such as functional loss, esthetic alterations, dental disorders, xerostomia, mucositis, hearing disorders, thyroid disorders, eye disorders, and osteonecrosis jaw, among others [18]

Therefore, alternatives for OC treatment are needed, which reduce or even abrogate CT's side

effects. Natural products are promising candidates in this context due to their low toxicity, safety and availability, making them an inexpensive, acceptable and therefore accessible approach [19,20].

According to US National Cancer Institute (NIH), most anti-tumor drugs are obtained from natural product [21]. Even the standard anticancer therapies, as vincristine, vinblastine, and paclitaxel, are of plant origin [22].

Natural products are eco-friendly, low-cost, safe, and less toxic compared with conventional chemotherapeutic methods. The ideal phytochemicals retrieved from natural products should be selective in their function & act on tumor cells without damaging normal cells. For these reasons, phytochemicals are considered suitable candidates for anticancer drug development, with apleiotropic action on target events occurring during oral carcinogenisis and involving several signaling cascades. [23]

Fig: 1 Treatment options for cancer [24]

Natural Products as Chemopreventive Agents in Oral Cancer

Currently, the pharmaceutical properties of these herbs are being vastly investigated. It is proposed that the medicinal herbs have the potential to treat several diseases such as cancer allergy, and diabetes. [25]

Cancer chemoprevention implies the use of natural or synthetic agent to inhibit, holdup, or regressing the tumor development process in public at high risk of the disease [26]. Several studies have documented the use of natural products in OC chemoprevention, and a wild range of compounds have been investigated as possible chemopreventive therapies in this pathology [27].

The anticancer activity of plant extracts or their isolates that has been studied IN-Vivo and IN-Vitro against different cancer cell lines. [28]

In the past decade preclinical studies on few phytochemical attracted many researchers & hence discussed in this review. [29,30]

In human tongue squamous cancer cell line, tea polyphenols reduce hTERT activity & inhibited cell proliferation and in cell lines derived from dysplastic leukoplakia and squamous cell carcinoma, they elicited G1 phase arrest. [31, 32] Some natural products that are used as Anticancer chemopreventive are given in **TABLE-1.**

Table 1- Natural Products in Oral Cancer Chemoprevention

Natural products	**Type of study**	**Cell line/animal model**	**Outcomes/key observations/mode of action**	**References**
Tea polyphenols	In Vitro	Tca8113	Reduced hTERT activity, inhibited cell proliferation, and showed arrest in G1 phase in cell lines derived from dysplastic leukoplakia and squamous cell carcinoma	[31,32]
Epigallocatechin-3 gallate	In Vitro	SCC-9	Inhibited invasion, epithelial-mesenchymal transition, and tumor growth in oral cancer cells	[33]
Curcumin	In Vitro In Vivo	CCL 23, CAL 27 and UM-SCC1	Inhibited growth of tumoral cells In Vitro and reduced tumor volume In Vivo by activation of NF-κB and suppression of TNF, COX-2, cyclin D1, c-myc, MMP-9, and interleukins Liposomal curcumin inhibited NFkappaB in a xenograft mouse model	[34,35]
Tea polyphenols/ curcumin	In Vitro	Normal oral epithelial cells MSK Leuk1 established from a dysplastic leukoplakia lesion	Exhibited synergistic chemopreventive effects by cell accumulation in S/G2M phase	[32]
Genistein	In Vitro	HN4, HNSCC	Downregulation of Cdk1, Cdc25C, cyclinB1, MMP-2, and MMP-9 and upregulation of p21WAF1 and Bcl-2 that produce cell cycle arrest and apoptosis	[36,37]
Resveratrol	In Vitro	SCC-VII, SCC-25, YD-38	Cell cycle arrest in the G2/M phase and apoptosis by enhancing the expression of phospho-cdc2 (Tyr 15), cyclin A2, and cyclin B1	[38]
Lycopene	In Vivo	4NQO albino rat model Lycopene 2.5mg/kg body weight	Increased expression of E-cadherin and β-catenin	[39]

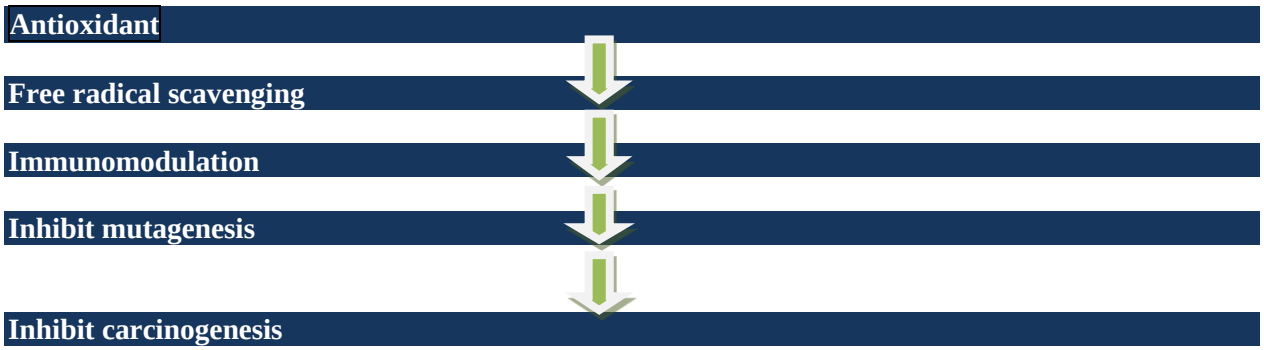
Azadirachtin and nimbolide limonoids	In Vivo	HPB carcinogenesis model	Upregulating p53, downregulating PCNA and GST-P, inhibits nuclear translocation of p50-p65 NF-κB Downregulation of PCNA, p53, and Bcl-2.	[40,41]
Black raspberry bioadhesive gel	Phase I/Phase II study	Patients with premalignant lesions	Reduced levels of iNOS and COX-2 protein in the altered epithelium Reduced the size of macroscopic lesions and microvascular density.	[42,43]

Antioxidants in oral cancer

Antioxidants neutralize free radicals by donating one of their electrons, ending the electron stealing reaction. Also antioxidants nutrients are stable in either form and thus, cannot become free radicals by donating an electron. [44]

Antioxidants acts by various mechanisms, that is, by anti-hormonal effect, an immune-enhancing effect, arrest of the cell cycle, and the cell differentiation. It also play a role in gene expression, suppression of proliferation, and angiogenesis, inhibit secondary modification, and development of oral cancer cell. [45,46,47]

Mode of action



Role of Antioxidants in oral cancer

Beta-carotene

Beta-carotene is a vitamin A precursor commonly found in dark green, orange or yellowish fruits and vegetables, such as spinach, carrots, sweet potato, mango, papaya, and oranges.

The main actions of beta-carotene include:

- Antioxidant and free radical scavenging.
- Immunomodulation, stimulation of increase in cell-mediated immune response (T-helper, NK cells, and cells with IL- receptors) due to increased monocyte expression and increased activity of tumor necrosis factor alpha.
- Inhibition of mutagenesis.
- Inhibition of cancer cell growth. [48]

In various oral premalignant lesions and conditions, serum beta carotene levels are shown to be decreased and thus its supplementation (30 mg/day) has led to the regression of these lesions. [49,50]

Retinoic acid (Vitamin A)

Carotene and animal products such as meat, milk, and eggs are the sources of Retinoic acid. Furthermore, in the intestine, retinoic acid is converted into retinal, and retinol hypervitaminosis occurs when the consumption exceeds the liver's capacity to store retinoids.

The main actions are, it:

- Inhibits keratinization and terminal differentiation of epidermal cells.
- Enhances cellular immunity.
- Arrests/reverses the progression of leukoplakia.
- Induces cytotoxic and cytostatic effects on cancer cells.
- Influences DNA, RNA, and gene expression.
- Interferes with carcinogenic stimulation and binding. [46,48,51]

L-Ascorbic Acid (L-ascorbic acid)

L-ascorbic corrosive (L-AA), the supposed L-ascorbic acid, is found in citrus natural products like kiwi, strawberries, papaya, and mango. The ongoing US suggested everyday stipend for ascorbic corrosive reaches somewhere in the range of 100 and 120 mg/each day for grown-ups. L-AA has an antioxidizing property and responds with the superoxide delivered because of the phones' typical metabolic cycles; this inactivation of superoxide restrains the development of nitrosamines during protein processing and maintains a strategic distance from harm to the DNA and cell proteins.

L-AA, aside from being a cell reinforcement, additionally has the accompanying activities:

- Decreases vitamin E corruption.
- Improves chemotaxis, phagocytosis, and collagen union.
- Hinders nitrosamine arrangement
- Improves detoxification by means of cytochrome p450.
- Blocks development of waste mutagens.
- Lessens oncogene articulation. [44,46,51]

α-tocoferol (vitamin E)

α-tocoferol (AT) is the most widely recognized and most dynamic type of vitamin E. It is found in plant oil, margarine, and green leaves. The suggested day as far as possible rates are 10 mg/day for grown-up men and 8 mg/day for grown-up ladies. α-tocoferol is a powerful cancer prevention agent at elevated degrees of oxygen, shielding cell films from lipidic peroxidation.

The fundamental activities of AT include:

- Free revolutionary rummaging.
- Support of film respectability, insusceptible capability.
- Restraint of disease cell development/separation.
- Cytotoxicity.
- It hinders mutagenicity and nitrosamine development.
- Forestalls DNA, RNA, and protein amalgamation in disease cells. [46,51,52]

Spirulina

The blue-green microalgae Spirulina, is utilized in everyday eating regimens of locals in Africa and America. Spirulina is the best food containing cancer prevention agents, phytonutrients, fundamental unsaturated fats, probiotics, and nutraceuticals. Spirulina is a magnificent wellspring of protein, beta-carotene, gamma linolenic corrosive, B-nutrients, minerals, chlorophyll, sulfolipids, glycolipids, superoxide dismutase, phycocyanin, and catalysts. Spirulina has no aftereffects and is non-harmful in nature. The supplements present in Spirulina support the safe framework and improve the body's capacity to create fresh blood cells to forestall illness and malignant growth. [53]

Green Tea

The anticarcinogenic properties of green tea polyphenols — fundamentally EGCG (epigallocatechin-3-gallate), which is the most naturally dynamic catechin — are reasonable a consequence of hindrance of cancer commencement and advancement, enlistment of apoptosis, and restraint of cell replication rates, hence hindering the development and improvement of neoplasms. The cell reinforcement capability of green tea polyphenols is straightforwardly connected with a mix of sweet-smelling rings and hydroxyl bunches that make up their construction, and is a consequence of the limiting and balance of free extremists by the hydroxyl gatherings. [54,55]

Epigallocatechin-3-gallate capture cells in the G0 - G1 stage, downregulate cyclin D1, increment p14ARFand/or p16 protein levels, and subsequently, balance out p53 and control apoptosis, and block angiogenesis by diminishing

the phosphorylation of the vascular endothelial development factor receptor (VEGF), and repress VEGF emission by cancer cells. [55]

Neem

Gallic corrosive, catechin, and epicatechin are phytochemicals connected with oral disease, which have a cancer-causing agent detoxifying protein, glutathione. Catechin can hinder the development of metalloproteases, diminishing the attack and relocation and instigating the apoptosis of disease cells. It has calming possible by suppressive enactment of atomic element κ-b (NFκ-b), which instigates the apoptosis of malignant growth cells.

Lycopene

It is perhaps of the most strong cancer prevention agent. Lycopene is a dazzling red carotene, carotenoid shade, and a phytochemical tracked down in tomatoes and other red foods grown from the ground, for example, red carrots, watermelons, and papayas. Lycopene has been speculated to forestall carcinogenesis and atherogenesis by safeguarding basic cell biomolecules, including lipids, lipoproteins, proteins, and DNA. In late examinations, the serum and tissue levels of lycopene have been demonstrated to be conversely connected with the gamble of bosom malignant growth, prostate malignant growth, coronary illness and oral premalignant sores. [46,48,57]

Lycopene can decrease the gamble of oral malignant growth, as it has been displayed to hinder the expansion of KB-1 human oral cancer cell by upregulation of connexin-43 (hole intersection protein) articulations, attending with improved hole junctional correspondence. [56,58]

As per different examinations, lycopene when given in a dose of 4-8 mg/day orally for a long time prompts an inversion of dysplastic changes in the oral leukoplakia, and 16 mg/day in oral submucous fibrosis. On a normal, the everyday admission of lycopene is assessed to be 3.7 mg. [59,60]

Curcumin

Curcumin is a yellow shaded phenolic color extricated from turmeric. It is very notable for its enemy of cancer-causing and other restorative action. Curcumin has antitumor action in the oral cavity, which can likewise repress cell development and prompt apoptosis in oral disease cells. Curcumin is likewise connected with downregulation of score 1, atomic variable κb (NF-κb), and articulation of cyclooxygenase-2 (COX2), fluid oxygen (LOX), iNOS (inducible nitric oxide synthase), framework metallopeptidase 9 (MMP-9), cancer putrefaction factor (TNF), chemokines, and other cell-surface bond particles, and cyclin D1. Curcumin can improve the disease battling force of the treatment with a growth rot factor-related apoptosis-instigating ligand (TRAIL). A prescribed everyday portion of up to 10 g can smother growth commencement, advancement, and metastasis. [56,61]

Mushroom

Mushrooms like shiitake, maitake, reishi, and some agaricus species battle against malignant growth and further develop the safe framework in light of the presence of certain glucans and polysaccharide peptides (proteoglycans) [Figure2]. Refined bioactive mixtures got from therapeutic mushrooms are a possibly new and significant wellspring of anticancer specialists. Four mushroom tests display amazing mutagenic and anticancer activity.[62]

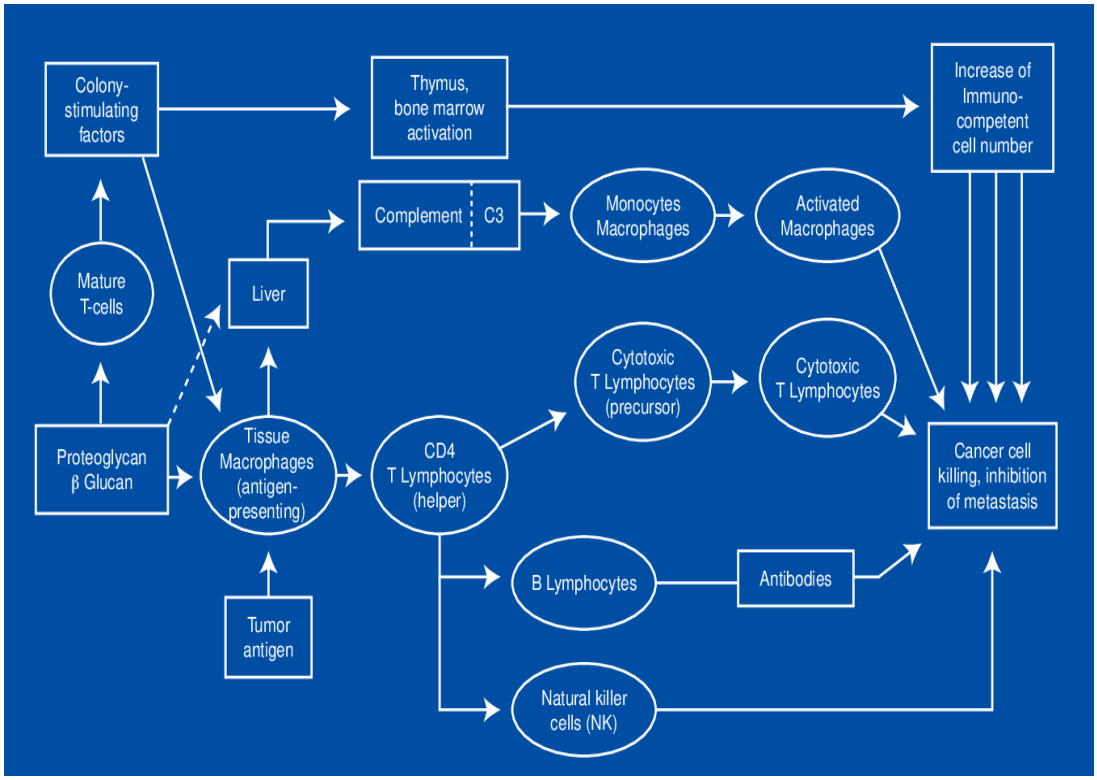


Fig: 2 Pathway of Immune upgrade by mushroom proteoglycans [63

Aloe Vera

Aloe Vera is a plant that has been utilized for clinical purposes for millennia. It is generally utilized for the therapy of different ailments, for example, oral ulcers, psoriasis, skin consumes, and frostbite, since it presents pain relieving, liver-assurance, antifungal, antidiabetic, calming, antiproliferative, anticarcinogenic, antiaging, and immunomodulatory properties. [65-67] Different investigations have shown the powerful free-revolutionary and superoxide anion action of three subsidiaries from Aloe vera, in particular, isorabaichromone, feruoylaloesin,
what's more, p-coumaroylaloesin. [68,69]

Tinospora cordifolia (Wild) Miers

Tinospora cordifolia, additionally called guduchi in Sanskrit, giloya in Hindi and heartleaf moonseed plant in English, is a bulky, smooth, mountaineering deciduous shrub missing bristles. The maximum typically used a part of the shrub is the stem, however roots also are acknowledged to include critical alkaloids. This shrub is typically determined in India, Myanmar, Sri Lanka and China. [70] According to historic Ayurvedic lexicons, T. cordifolia is likewise noted as “amrita”. The term “amrita” is ascribed to this plant because of its cappotential to impart youthfulness, energy and longevity.[71] T. cordifolia successfully kills HeLa cells in vitro, suggesting its cappotential as an anticancer agent. A dose-established boom in mobileular demise turned into determined in HeLa cells handled with T. cordifolia extract in comparison to the controls [72]. The anticancer interest of dichloromethane extract of T. cordifolia withinside the mice transplanted with Ehrlich ascites carcinoma has been demonstrated. T. cordifolia extract confirmed a dose-established boom in tumor-loose survival with maximum range of survivors determined at 50 mg/kg dose. [73]

Phyllanthus amarus Schumach. & Thonn

Phyllanthus amarus is determined in tropical Asia, mainly in hotter components of India and is called bhumyamalaki in Sanskrit, jaramla in Hindi and stone breaker in English. The entire

plant, leaves, roots and shoots are reportedly used for his or her medicinal values. The chemoprotective houses of this plant can be associated with its cappotential to inhibit metabolic activation of carcinogenic compounds, result in mobileular cycle arrest and intrude with DNA repair [74] . The extract of P. amarus inhibited the interest of cdc 25 tyrosine phosphatase, that's a key enzyme worried in mobileular cycle regulation . The extract of P. amarus resulted withinside the inhibition of the interest of topoisomerase I and II in Sacchromyces cerviacae mutant mobileular cultures [75]. P. amarus extract has additionally been stated to have anti-angiogenic results in mice bearing Lewis lung carcinoma with proof to intrude with the migration of vascular endothelial cells. [76]

Annona atemoya Mabb./ Annona muricata Linn

Annona atemoya/muricata is a local of Caribbean, Central and South America. It is likewise typically grown in South East Asia mainly in japanese a part of India. This plant is historically called mamaphal in Hindi and sour-sop of America in English. The components of the plant which can be typically used for medicinal functions are the root, bark, leaf and fruit. The fruit of A. atemoya includes bullatacin (chemical shape proven below), an acetogenin acknowledged to have antitumor houses. Bullatacin induces chromatin margination and tumor mobileular condensation, accompanied with the aid of using apoptosis [77]. A. atemoya includes annomuricins particularly A and B, that have proven cytotoxicity in human stable tumor mobileular strains A-549 lung carcinoma, MCF-7 breast carcinoma, and HT-29 colon adenocarcinoma mobileular strains [78]. A. atemoya includes numerous different acetogenins which have additionally been proven to selectively result in mobileular demise in tumor cells in vitro [79]. In particular, annonaceous acetogenins had been determined to supply mobileular demise withinside the human hepatoma mobileular line HepG2 and hepatoma 2.2.15 cells [80].

Bitter Melon And Oral Cancer

Bitter melon (Momordica charantia) or sour gourd, balsam pear, or karela, has been recognized for a long time for the remedy of diabetes[90, 92] . The plant belongs to the own circle of relatives Cucurbitaceae and grows in tropical and sub-tropical areas of Asia, Africa and South America. The crude extract or remoted compounds additionally display anti-lipidemic, antibacterial, antifungal and anti-HIV activities[91,93,94]

It is a abundant supply of phytochemicals, maximum of that have capability organic activities. The predominant chemical materials are categorised as cucurbitane-kind triterpenoids, cucurbitane-kind triterpene glycosides, phenolic acids, flavonoids, crucial oils, fatty acids, amino acids, sterols, saponins and proteins; amongst those, the cucurbitane-kind triterpenoids are the maximum prevalent[93,100] . The cucurbitane-kind triterpenoids (momordicines I and II) and triterpene glycosides (momordicosides K and L) make contributions to the bitterness of the plant[94] .

Molecular mechanisms of bitter melon in prevention of OSCC are summarized below:

Cell cycle modulation

Deregulation of the mobileular cycle is one of the main activities in OSCC[96,97] . This is finished via way of means of common modulation of mitogenic and anti-mitogenic reaction regulatory proteins together with cyclins, cyclin-structured kinases (CDKs), CDK inhibitors [p21 (WAF1/ CIP1), p27 (KIP1), p16 (INK4a)], and retinoblastoma tumor suppressor protein (RB)[96] . A targeted transcriptomic array accompanied via way of means of protein degree validation confirmed that BME inhibits the expression of mobileular cycle inducers cyclin D1 and survivin, and turns on mobileular cycle inhibitors p21 and p27 in OSCC cells [95] . Down-law of transcription factor E2F, proliferating mobileular nuclear antigen (PCNA), mini-chromosome renovation complex thing 2 (MCM2), karyopherin subunit alpha 2 (KPNA2) and upregulation of ataxia telangiectasia mutated (ATM) and ataxia telangiectasia and Rad3-associated protein (ATR) are additionally obvious following BME treatment. Similar

consequences had been additionally suggested in breast and prostate most cancers prevention via way of means of BME ensuing in both S or G2-M segment arrest withinside the mobileular cycle[98,99] . Thus, mobileular cycle modulation is an crucial occasion withinside the prevention of oral most cancers via way of means of BME.

Modulation in cell signaling

Alteration in signaling activities prefer unregulated proliferation, motility and survival of most cancers cells [101], Many receptor-ligand signaling activities had been investigated in oral most cancers, and a number of the ones constitute capability goals for most cancers therapy. BME treatment inhibited the expression of a few key regulatory genes of c-Met (MET proto-oncogene) signaling along with the receptor tyrosine kinase c-Met, sign transducer and activator of transcription 3 (STAT3), c-Myc proto-oncogene and myeloid mobileular leukemia-1 (Mcl-1) in pre-scientific fashions of OSCC. Cancer, and a number of the ones constitute capability goals for most cancers therapy. BME treatment inhibited the expression of a few key regulatory genes of c-Met (MET proto-oncogene) signaling along with the receptor tyrosine kinase c-Met, sign transducer and activator of transcription 3 (STAT3), c-Myc proto-oncogene and myeloid mobileular leukemia-1 (Mcl-1) in pre-scientific fashions of OSCC.[102]

Yoga in therapy of disease

Yoga as a lifestyle, including diet and way of life as well as yogasanas, pranayama, and contemplation contributes toddler he counteraction and long haul reduction from disease. Yoga can invert epigenetic changes against persistent infections. Yoga treatment might diminish the possibilities of carcinogenesis. Actual activity can kill the arising destructive cells normally. Additionally performing breathing activities like pranayama and yoga stances, assist people in managing malignant growth in a quiet way. Keeping a sound resistant framework is essential to battle the destructive cells emerging in the body, as stress debilitates the safe framework; yoga and contemplation are prescribed to reduce pressure. [103,104]

SWOT Analysis

A SWOT outline (Figure 5) was built with the plan to portrayed qualities, shortcomings, valuable open doors, and dangers of utilizing regular items for the counteraction/treatment of OM. In spite of the huge advances made around here, more examinations are expected to guarantee that these plans arrive at the drug market, and few have been distributed in regards to this subject with regular items. [105]

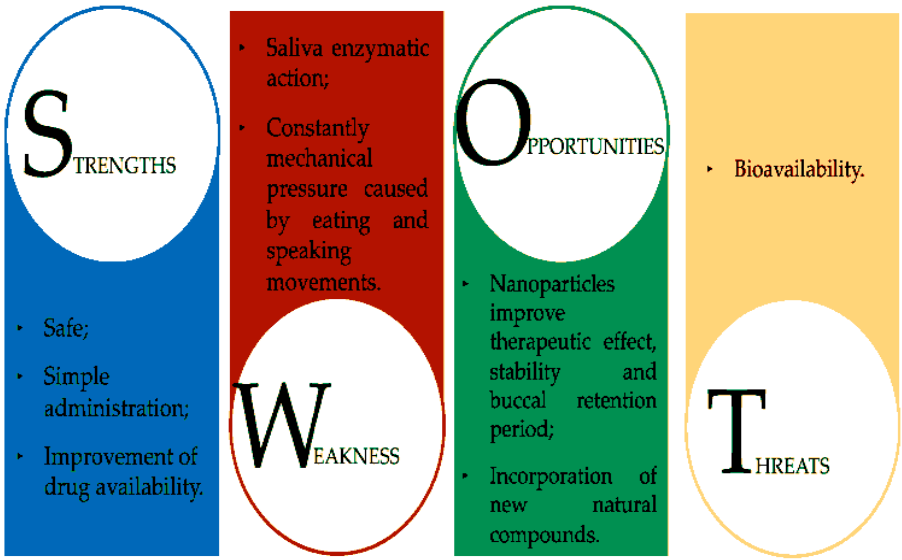


Fig: 5 SWOT investigation for the conceivable utilization of normal items to forestall/treat OC [106]

2. Conclusion

An extraordinary assortment of regular items are the subject of gigantic interest in malignant growth chemopreventive examination as the idea of using such items and their fixings, alone or in blend with cutting edge disease treatment, is at the very front of flow drug research. A few concentrates as well as mixtures have been displayed to have chemopreventive and antitumoral potential in OC cells, prompting their apoptosis by extraneous and natural pathways and hindering their expansion by following up on designated spots prompting cell capture in the G1/S stage. The helpful capability of these normal items is put together not just with respect to their capacity to hinder cancer cell expansion and prompt apoptosis yet additionally on their capability to restrain metastasis-related processes fundamentally multiplication, movement, attack, and MMP-2/MMP-9 action in OC cells, with EMT hindrance. Thusly, normal items are great contender for future enemies of metastases treatments, in this manner diminishing mortality by disease.

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