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A Review On Oral Cancer Disease

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Abstract: This article focuses on saliva as a diagnostic medium of choice and the various biomarkers that are elevated in oral cancer. The outcome of Research proves that 90 % of the oral cancers are oral squamous cell carcinoma. The causative factors, risk factors, and screening for oral cancers are elaborated. Salivary biomarkers can be classified into genomic and protein bio markers. Among Genomic biomarkers the role of micro RNAs is specified and these nitidity of various protein biomarkers such as matrix metalloproteinases, cytokines are studied.

Index Terms :

- Minor salivary gland
- Mucosal Melanoma
- Sarcomas
- Squamous Cell Carcinoma

Introduction: An ulcer can be defined as a loss of continuity in the skin, mucous membrane or oral mucosa. Head and neck cancers are cancers that statin the tissues and organs the head and neck they include cancers of the larynx (voice box), throat, lips, mouth, nose, and salivary glands Most types of head and neck cancer begin in squamous cells that line the moist surfaces inside the head and neck (for example, the mouth, nose, and throat). Tobacco use, heavy alcohol use, and infection with the human papillomavirus (HPV) increase the risk of many types of head and neck cancer The risk factors for oral cancer depends on the gender, age, Prolonged Sun exposure, tobacco use and alcohol, diet, HPV infection Are can't chewing, and lodging the betel quid of the are cannot in the buccal vestibule leading to pre-cancerous and cancerous lesions due to chronic irritation and significant changes.

In the oral mucosa adjacent or under neath it. This results in Extrinsic stains loss of esthetics requiring scaling and oral prophylactic measures. The most common symptom is asoreoranulcer in the mouth that does no that easily and which discharges or bleeds either on examination or spontaneously. Screening

for oral cancer should include a thorough History and physical examination. The clinician should visually inspect and palpate the head, neck, oral, and pharyngeal regions. This procedure involves digital palpation of neck node regions.

Types OF Cancer:

- Lymphoma
- Minor salivary gland
- Mucosal Melanoma
- Sarcomas
- Squamous Cell Carcinoma

Stages of cancer

- Stage1: The Tumor is 2Cmor smaller
- Stage2: The Tumor is between2- 4
- Stage3: The Tumor is Larger than 4 Cm
- Stage4: Tumor are any size and the cancer cell have spread tissue

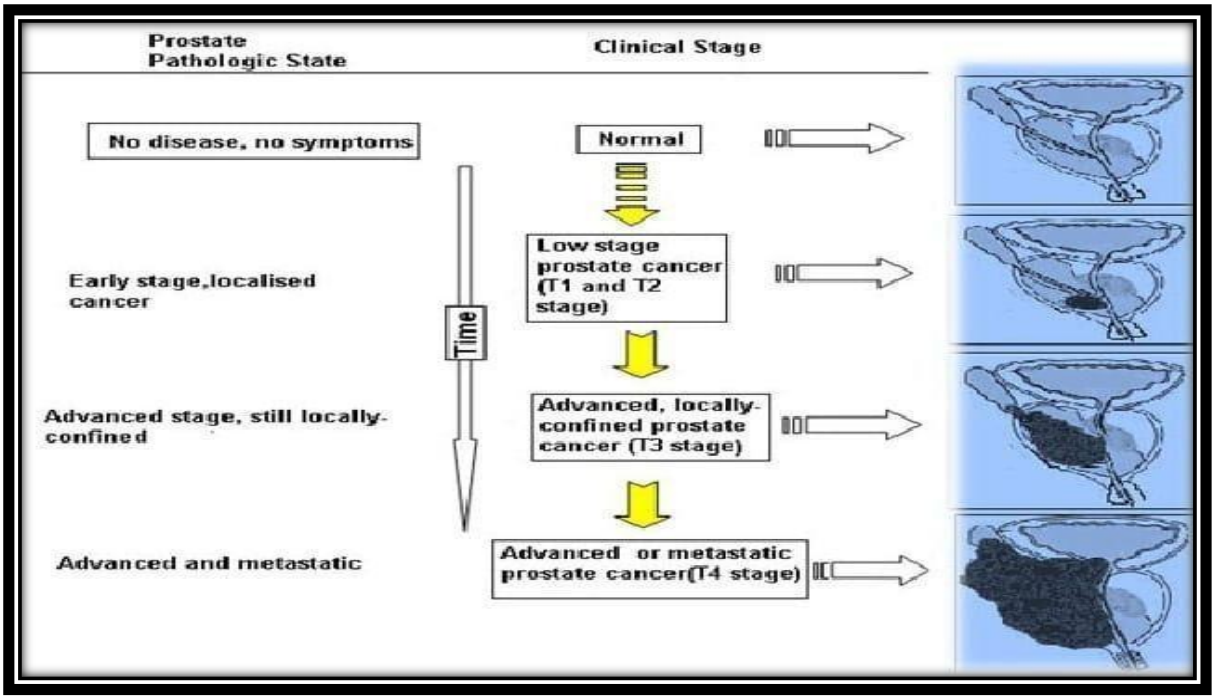


Fig No.1

Risk Factors:

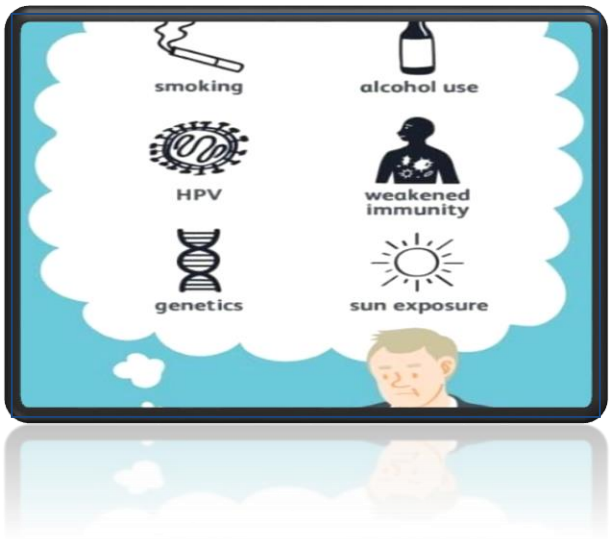
Tobacco:

All forms of tobacco - cigarettes, pipes, cigars, and smokeless tobacco have been implicated in the development of OC. While tobacco confers the highest risk for OC of the floor of the mouth also, it is associated with an increased risk for all sites of OC. Tobacco use is responsible for 90% of OC deaths in males.

Alcohol

Alcohol use is as second in dependent major risk factor for the development of OC. For non-smokers it is the most important risk factor. Above 30 grams of alcohol per day, risk increases linearly With amount of alcohol consumed.

In addition to tobacco use, the use of chewing products such as betel nuts, paan, chaalia, gutka, naswar, and are cancer increases the risk for OC; these products are socially acceptable in South east Asia, the South Pacific Islands, and India.



FigNo.2

Fig No.3

Shammah: Shammah, a traditional smokeless tobacco habit in the Arabian Peninsula, has a significant association between the prevalent ceofleukoplakia and the daily duration of shammah application in a dose-dependent manner.

Marijuana:

Poly microbial supra gingival dental plaque is a possible independent risk factor, as it possesses a relevant mutagenic interact on with saliva, and thus oral health may be a co-factor in the development of OC. The carcinogenic properties of marijuana a smoke are with mutagen sensitivity and other risk factors to increase where diets have been supplemented have shown some beneficial effect on pre-malignant conditions and reducing the risk OC, but further work into diet and the role of chemo prevention in oral cancers is needed.

UV Light:

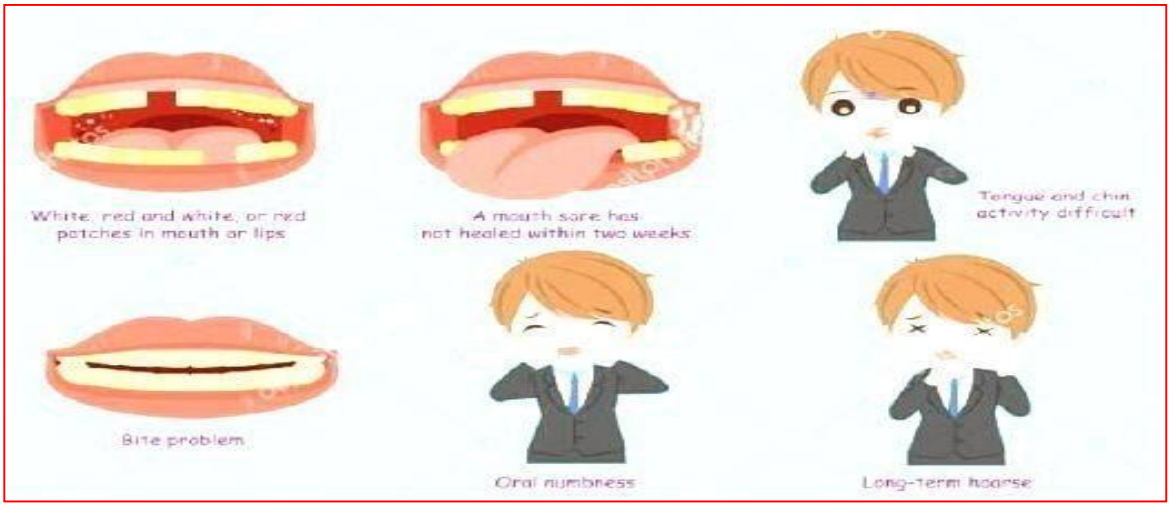
Solar irradiation is a major risk factor for cancer of the lip. The vast majority of lip cancer occur on the lower lip and many patients have outdoor occupations where sun exposure is increased. Lip cancer is three times more common in men than women which may be an effect of occupation, smoking and sun-exposure.

Irritation. :

Although it has been suggested that chronic irritation to the lining of the mouth from poorly fitting or Defective completed ensures may be a risk factor for OC, the majority of studies have shown no correlation

Dental Plaque:

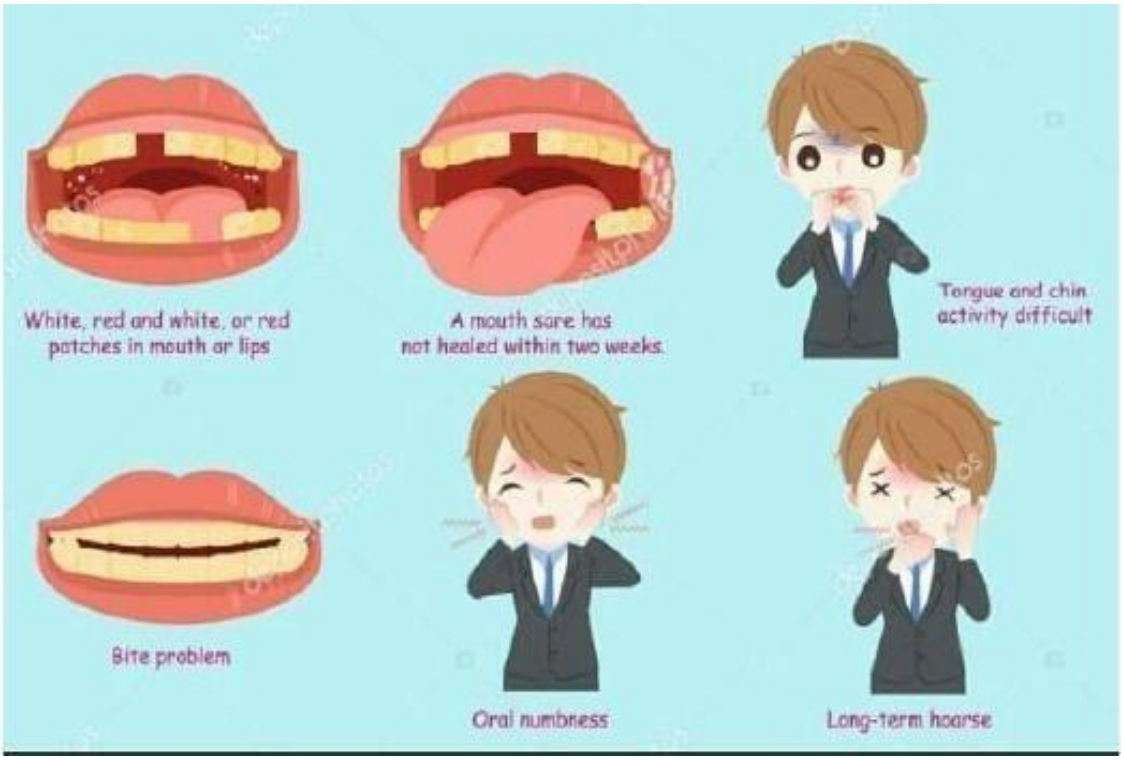
Ethyl alcohol is added to mouth rinses as a solvent for other ingredients and as a preservative. Study shows that cancer was not statistically associated with mouthwash use in alcohol or tobacco users. Currently, there is insufficient clinical evidence to suggest a relationship between ethyl alcohol found in mouth rinses and OC.



Etiology: The etiology of oral cancer in man is unknown. However, several pre-existing conditions have Been found with such frequency in patients with oral cancer that they may be considered, at least in part. As contributory factors. For instance, chronic irritation seems to be related to the development of cancer, whereas a single episode of trauma does not. Other factors which may lead to the development of oral cancer include: El Ionizing radiation at therapeutic, not diagnostic, dosage levels. Fortunately, because of strict erred bio therapeutic guidelines, few patients are today exposed to sufficient quantities of ionizing radiation to produce cancers of the oral cavity. E l Chronic exposure to actinic radiation. Chronic exposure to the sun is a significant factor in the development of cancer of the lower lip, the most common form of oral cancer. The high Inci lip, as well as epidermis carcinoma of the lip in hot climates attests to the etiologic significance of long- term exposure to sunlight. Apparently, repeated exposure to ultraviolet sol array so vera period of 15- Years results in atrophic alterations of the exposed aspect of the lower lip, which may develop. The carcinogenic action of solar rays varies according to intensity Dr. Oster amp is in general dental practice in St. Louis, Missouri. Dr. Whitten is Associate Professor and Chairman. Department of Pathology, School of Dental Medicine, Southern Ill ion is University. And length of Exposure and is probably limited by pigmentation. In black people, for example, epidermis carcinoma of the lip is extremely rare. El The use of chewing tobacco and snuff. The prolonged use of these agents may lead to benign, premalignant and malignant lesions of the base of the tongue and the buccal mucosa. These habits, which involve holding unburned tobacco directly against the tissue in one area of the mouth, may produce a local concentration of the chemical constituents of tobacco, resulting in changes in the mucous membrane. In addition, other tobacco-related habits, such as chewing betel nut and pan, have been as sociated with dysplastic or neoplastic disease as a result Of chemical irritation. A number of toxic agents, such as the lye used in the betel nut cud, have also been shown to have a contributory relationship to oral cancer. El The chronic ingestion of alcohol. This has been found to be a causative factor in the development of oral cancer, especially cancer of the floor of the mouth and tongue The decreased incidence of oral cancer in Great Britain in the last few years, in direct proportion to a decrease in alcohol consumption, supports this association. El The action of specific infectious agents. Atrophic luetic gloss it is found in tertiary syphilis has, for instance, been associated with the development of cancer of the tongue. Epidemiological studies have found an increased incidence of oral cancer for cigarette smokers, as well as pipe and cigar smokers. Long- term exposure to the chemical carcinogens in tobacco and the trauma from heat and drying generated by Cigarette smoking are of etiological significance in the development of cancer of the oral cavity and pharynx.

Symptoms:

- A sore, irritation, lump or thick patch in the mouth, lip, or throat
- A white or red patch in the mouth
- A feeling that's a men thing is caught in the throat
- Difficulty chewing or swallowing



DIAGNOSIS :

Most oral cancer screening programs include the simple visual inspection, whereas others attempt the use of toluidine blue, brush biopsy (exfoliated cytology) chemiluminiscence and fluorescence imaging. The last three screening methods in fact deal with the diagnosis of lesions that have already been detected by the Patient, dentist or other clinician but a definitive diagnosis can only be made by a tissue biopsy. Diagnosis can be delayed by several months or more if the clinician treats the patient's complaints empirically with drugs instead of providing a thorough physical examination and workup Patients with complaints lasting longer than 2-4 weeks should be referred promptly to an appropriate specialist to obtain a definitive diagnosis. If the specialist detects a persistent oral lesion, a biopsy should be performed without delay. There are invasive and non-invasive methods of detecting oral cancer.

Biopsy is defined as removal of tissue from a living in dividual for diagnostic examination. The health history, history of the lesion, clinical examination, radio graphic that the levels denote the systemic health and disease status. The first report of saliva as a diagnostic medium for oral cancer was published by Liao et al. whom identified mutations in exon4, condon63 in 5 out of 8 patients with oral squamous cell carcinoma. Saliva can be utilized for early detection of oral cancer as this body fluid maintains continuous contact with these lesions. Diagnosis of OSCC is currently based on biopsy test, which is an invasive method. There is a need for developing.

Diagnostic Test: -

1) Biopsy

A biopsy is the removal of a small amount of tissue for examination under a microscope. Other tests can suggest that cancer is present, but only a biopsy can make a definite diagnosis of colorectal cancer. A pathologist then analyses the sample(s). A pathologist isa doctor who specializes in interpreting laboratory tests and evaluating cells, tissues, and organs to diagnose disease. A biopsy may be performed during a colonoscopy, or it may be done on any tissue that is removed during surgery. Sometimes, a CT scan or ultra sound (see below) is used to help perform a needle biopsy. A needle biopsy removes tissue through the skin with a needle that is guided in to the tumor

.

2) Computed tomography (CT or CAT) scan.

A CT scan takes pictures of the inside of the body using x- rays taken from different angles. A computer combines these images into a detailed,3- dimension a image that shows any abnormalities or tumours. A CT scan can be used to measure the tumour's size. Sometimes a special dye called a contrast medium is given before the scan to provide better detail on the image. This dye can be injected into a patient's vein or given as a pill or liquid to swallow. In a person with colorectal cancer, a CT scan can check for the spread of cancer to the lungs, liver, and other organs. It is often done before surgery (see Types of Treatment).

3) Magnetic resonance imaging (MRI).

An MRI uses magnetic fields, not x-rays, to produce detailed images of the body. MRI can be used to measure the tumour's size. A special dye called a contrast medium is given before the scan to create a clearer picture. This dye can be injected into a patient's vein or given as a pill or liquid to swallow. MRI is the best imaging test to find where the colorectal cancer has grown.

4) Ultra Sound:

An ultrasound uses sound waves to create a picture of the internal organs to find out if cancer has spread. Endorectal ultrasound is commonly used to find out how deeply rectal cancer has grown and can be used to help plan treatment. However, this test cannot accurately detect cancer that has spread to nearby lymph nodes or beyond the pelvis. Ultrasound can also be used to view the liver, although CT scans or MRIs (see above) are better for finding tumors in the liver.

5) **Chest X-ray**: An x-ray is a way to create a picture of the structures inside of the body, using A small amount of radiation. An x-ray of the chest can help doctors find out if the cancer has spread to the lungs.

6) **POSITRON EMISSION TOMOGRAPHY (PET) OR PET-CT SCAN.**

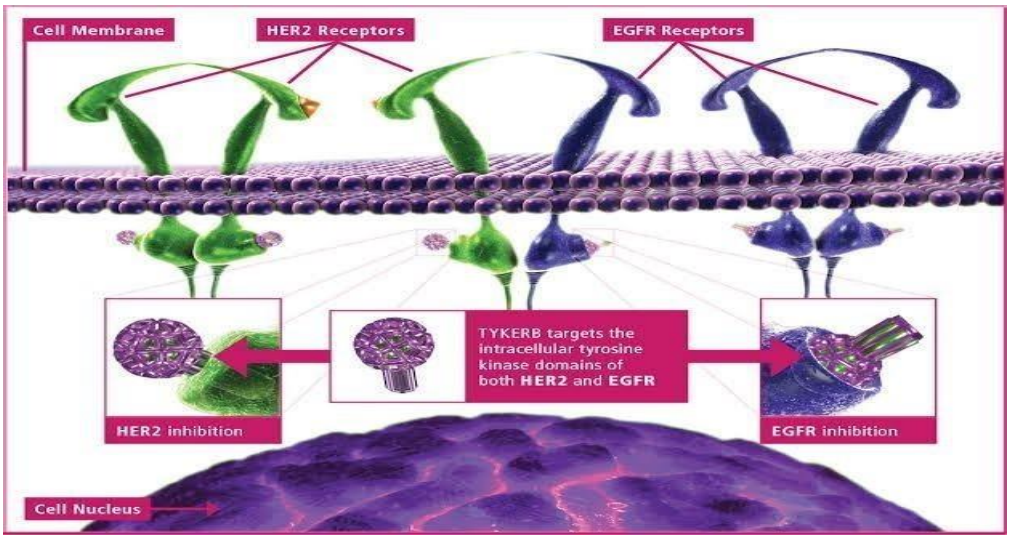
A PET scan is usually combined with a CT scan (see above), called a PET-CT scan. However, you may hear your doctor refer to this procedure just as a PET scan. A PET scan is away to create pictures of organs and tissues inside the body. A small amount of a radioactive sugar substance is injected into the patient's body. This sugar substance is taken up by cells that use the most energy. Because cancer tends to use energy actively, it absorbs more of the radioactive substance. A scanner then detects this substance to produce images of the inside of the body. PET scans are not regularly used for all people with colorectal cancer, but there are specific situations in which your doctor may find them useful.

- **Drug Use in Treatment of Oral Cancer**

1) Tykerb
2) Xeloba
3) Capecitabine
4) Methotrexate

1) Tykerb

Mechanism of Action is an inhibit of the intracellular tyrosine kinase domains of both epidermal growth Facture receptor



Side Effect

- Neuse
- Upset Stomach
- Mouth Sore throat
- Trouble Sleeping occur

Serious Side Effect

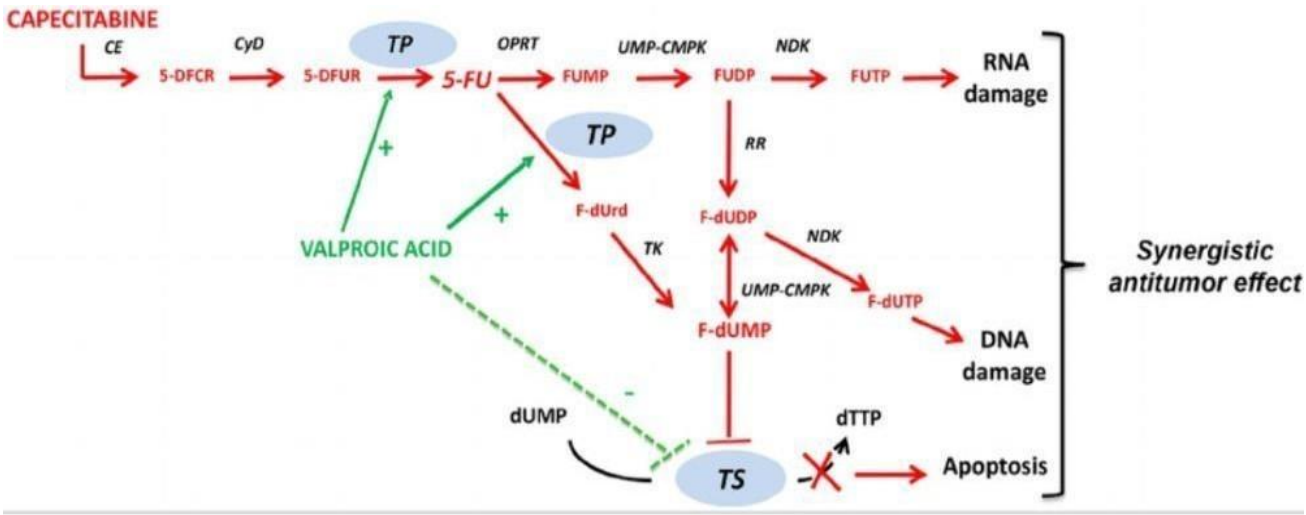
- Pain or redness on the palms of your hands or so lies of your foot
- Hair loss

Dose 1-21 Days Continuously

Marketing Formulation:

2) **Capecitabine** :

Mechanism of Action: The triphosphate from zalcitabine inhibits HIV receptor Transcriptase by competing for incorporation



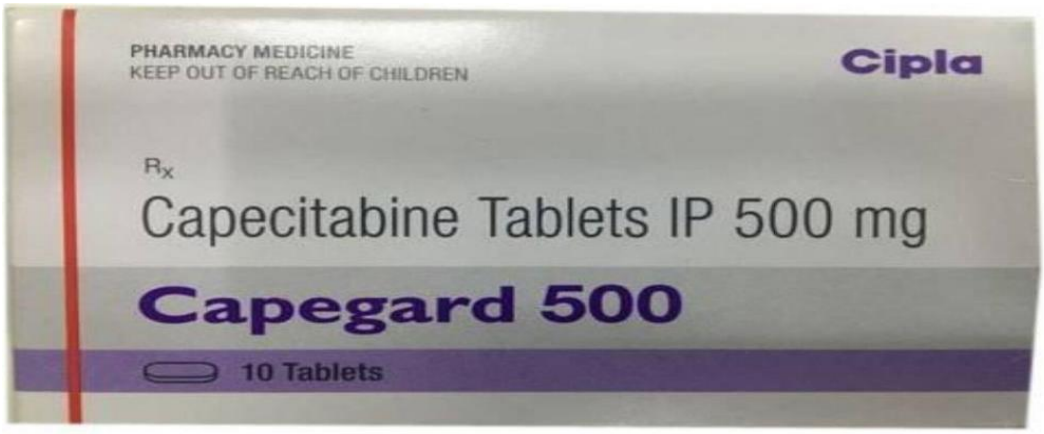
Side Effect

- Nausea
- Upset Stomach
- Mouth Sore Dry Skin
- Trouble Sleeping So occur

Serious Side Effect

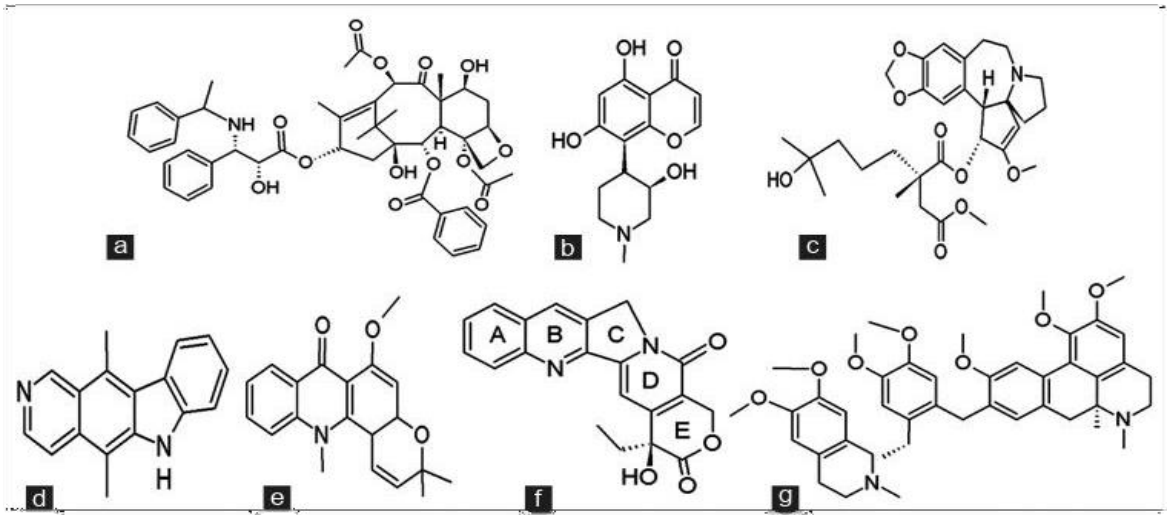
- Pain or redness on the palms of your hands or so lies of your foot
- Hair loss

Marketing Formulation:
Dose- Twice a Day



- **Including Some-Drug Taxol :**Taxol renamed Paclitaxel and sold under the trademark Taxolis the most successful anticancer agent developed from trees. The alkaloid –natural product Taxol

was isolated for the first time from the bark Cancer Institute (NCI) Screening program Research Triangle Institute Together with other baccatins, the natural product taxol is isolated at low level from needles, seeds, and bark of T. breve folia, in addition to other Taxus species, Few gymnosperms, angiosperms, and several endophytes, as reviewed The yield quantity varies with genotype, tissue, season, and environmental factors endophytes And culture condition storage condition and extraction technique used the poor solubility and limited supply hampered



3) Camptothecin:

Camptothecin is mono terpene pent acyclic quinoline alkaloid discovered from leaves extracts of Camptotheca acuminata during screening of natural products for anticancer drugs development at RT Iin an extensive screening program of the NCI on anticancer agents The alkaloid is produced in Nothapody tesnimmoniana at higher yield quantity than other plant natural sources Besides plant sources, camptothecin is produced by many endophytes isolated from camptothecin-producing host plants as well as when the endophytes were grown in culture media Camptothecin and congeners are S-phase-specific drugs that show spectrum activity on neoplastic cells. The tumor cells need prolonged exposure to camptothecin concentration exceeding least threshold to exert an effect During bioactivity testing of camptothecin, it showed a remarkable prolongation of mice with leukemia cells Walker WM tumor, leukemia. The success encouraged preliminary and clinical trials with a Result antre markable anticancer activity. However, Side effects of low solubility and high adverse drug reaction halted further studies During phase I trials, primarily in gastroin test inal tumors, the partial response for a short duration with unpredictable side effects of diarrhea, vomiting, severe hemorrhagic cystitis, and myelosuppression was shown. In clinical trials carried out in the USA, very poor response in patients was recorded however, in China, effective response in intestinal, gastric, bladder carcinoma and head an

Acronycin :

Acronycin was isolated for the first time from the bark of small Australian tree Paronychia baueri and the chemical structure determined. Later, several derivatives were isolated from the bark of Sarcomelico pesimplici folia, Sarcomelico peargyrophylla, Sarcomelicopeglauca, leaves and bark of Sarcomelico pedogniensis, Sarcomelico pepembaiensis, As well as aerial parts of Melicopeleptococca Since then, structural derivatives have been isolated from members of the family Rutaceae, several congeners developed, and successful total synthesis achieved. Acronycin and congeners show diverse bioactivities including anticancer effect and are attracting research interest in recent years due to the wide range bioactivities. The biological activities are thought to occur due to the planarity of the aromatic structure of the molecule that intercalates into DNA, leading to interference with cellular replication machinery during replication the alkaloid And congeners show a selective inhibition of many human pathogenic viruses including DNA and RNA viruses Inhibitory effects of the molecules against cellular and viral enzymes with intercalation ability into nucleic acid has been shown 'They showed cytotoxicity on melanoma, colon, lungs, murine tumor cell lines, breast, and other solid tumors but slight activity against murine leukemia models. Because of the cytotoxicity of acronycins, phase I– II clinical trials to evaluate their safety in patients with multiple refractory myelomas were per formed with limited success in the invitro models, 'acronycin caused swelling and destruction of Golgi complexes with less consistency on mitochondria of murine leukemia cells, cell layer culture of cervical Carcinoma, melanoma, and SV40-induced hamster tumor cells. The mechanism of action of acronycin and congeners is yet to be established at molecular level, but they Inhibited incorporation of cytidine, uridine, and other nucleosides, Leading to inhibition of nucleoside transport across plasma membranes and antitumor activity. Studies on SAR to uncover pharmacological activity resulted in understanding the structural features responsible for the anti-tumor activity and necessity of their arrangements Chemical structure of acronycin neck cancers was observed.

Thalicarpine :

Thalicarpine is a novel dimeric alkaloid isolated from roots of several species belonging to genera Thalictrum. The alkaloid was synthesized, and structural configuration determined Thalidasine, thalifoetidine, thalamelatine, and barbering alkaloids showed cytotoxicity in monolayer-cultured KB cells the thalicarpines inhibited protein synthesis in monolayer KB cells and Walker 256 carcinoma of rat, synthesis of DNA, RNA, proteins in cultured L1210 cells, as well as first step in th ebiosynthesis of nucleotide triphosphate Partial and reversible DNA synthesis inhibition occurred due to inhibited hymidine incorporation into cells, Inhibited RNA synthesis reversed when cells were washed free of thalicarpine, while inhibited protein synthesis occurred at first stage of biosynthetic scheme. Research ratovarian tumor cell lines howed higher cytotoxicity of the alkaloids incisplatin-resistantce lines than insensitive parental line.

Management Of Oral Cancer:

Oral cancer is a serious disease that is on the increase. The most pressing need is early recognition and referral for specialist treatment. Too many cases present with advanced tumors. Radiotherapy and surgery remain the primary modalities of curative treatment, but understanding of tumor pathology and developments in surgical and radio therapeutic technique have combined to produce a rational approach to management. In many instances 'radical' methods of

POST OPERATIVE RADIO THERAPY ± CHEMOTHERAPY

-Risk profile and indications for adjuvant treatment Primary surgery is the traditional approach for respectable OSCC in most centers. For patients with unfavorable pathological features, post operative radiotherapy (PO RT) or post operative concurrent chemo-radiotherapy (POCRT) have been shown to improve LRC and survival in several clinical trials. General indications for PORT include: T3 or T4 tumor; compromised(<5 mm from the inked surface of the specimen); presence of lymph-vascular invasion (LVI) and/or peri- neural invasion (PNI); and positive lymph nodes with or without extra capsular in vasion (ECE)The presence of multiple risk factors is common in OSCC. To understand the loco-regional recurrence risk profile, Langendijk, et al. studied 801 head-and-neck cancer patients (73% of whom had OSCC) who underwent PORTin1985-2000. They did not include their most favorable cases that did not require PORT in the report. A recursive partition inanely sized dressing loco-regional recurrence stratified patients into three risk groups: a) intermediate-risk: clear resection margins and no ECE, b) high-risk: T1, T2 and T4 tumor with close or positive margins or one pathological positive lymph node with ECE, c) very high-risk: T3 tumor with close or positive surgical margins or multiple pathological positive lymph nodes with ECE or an N3 neck For the latter two groups, the 5-year LRC with PORT was unsatisfactory (78% and 58%, respectively). The authors concluded that more intensive approaches, such as POCRT with concurrent chemotherapy should be con side red for these two sub-groups. Pathological stage I-II disease with sufficiently clear resection marginsis generally considered low-risk and does not require PORT Studies suggest that PNI alone appears to be nonproductive for recurrence However, the presence of LVI or microscopic tumor foci in muscle increased the risk of recurrence and PORT should be considered. Tumor thickness, or alternative synonyms such as “depth of invasion” or “tumor depth”, has been consistently identified as a predictor for cervical lymph node metastasis Recent studies have shown .

Conclusion:

Oral cancer continues to be a deadly disease for more than 50% of the cases diagnosed every year. This is due to the fact that most of these cases are diagnosed when they have already progressed to the advanced stage. Various studies have revealed that there is a lack of awareness about oral cancer, its signs and symptoms among the general population across the globe. Educating the general population about oral cancer is a must to combat mortality and morbidity arising outofit. It is necessary to have an understanding about the risk factors, Research needs to be done on the natural history, clinical course of the disease, particularly on those precancerous lesions which turn cancerous over time. Invention of new tumor markers with high sensitivity and specificity can lead to early detection of oral cancer and can minimize the damage. Continued research needs to be done to improve the diagnostic and treatment modalities for oral and oropharyngeal cancers, which can not only reduce the mortality but also enhance the quality of life of the patients.

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