1. INTRODUCTION

1.1 ORAL HEALTH

The physical and mental health as well as immune system to fight against diseases is considered to be healthy. Oral health contributes a major part in maintaining overall health and the quality of life in humans. According to WHO, oral health is a “state of being free from mouth and facial pain, oral and throat cancer, oral infection and sores, periodontal (gum) disease, tooth decay, tooth loss and other diseases and disorders that limit an individual capacity in biting, chewing, smiling, speaking and psychological well-being”[1]. Oral diseases of humans are one of the major issues particularly in low-income populations. It is common among 15 years (63.1%) and 35-44 years affects by 80.2% [2]. The increase in number of oral diseased patients has been leads to creating awareness regarding the oral hygiene, healthy eating, periodic checkups and fluoride prophylaxis [3]. Hence, an adequate knowledge of the oral health is essential to prevent or overcome many oral diseases in humans [4-6].

1.1.1 NORMAL FLORA

Oral cavity contains variety of microbial species such as bacteria, fungi, protozoa and rarely virus, of which bacteria and fungi causes the common oral infections in humans [7-10]. Microbes distributed in various parts of oral cavity such as palates, cheeks, tongue, teeth and gingiva. Aerobes are widely distributed around the oral cavity whereas anaerobes majorly present in gingival crevice area. The microbes present in oral cavity are highly influenced by various environmental factors such as pH, oxygen concentration, nutrients, temperature, host immunity and host genetic factors etc.
Around 750 species of microbes are reported to be present in the oral cavity. The common bacterial species are *Streptococcus, Bifidobacterium, Corynebacterium, Lactobacillus, Neisseria, Camphylobacter, Desulfovibrio, Desulfobacter, Fusobacterium, Haemophilus, Actinomycetes, Peptococcus* etc.,

The major predominant species are *Candida, Lactobacillus, Streptococcus mitis, S. oralis* and *S. salivarius*. The normal flora usually prevents the host from other pathogens and infections and also helps in metabolism. For example, Salivaricin, a compound produced by *S. salivarius* are active against Group A Streptococci pathogen [11-13].

### 1.1.2 OPPORTUNISTIC PATHOGENS

The commensal present in the oral mucosas rarely cause invasive diseases in healthy humans. But non-beneficial microbes have a direct link to oral infections in particular conditions like immune-compromised [14]. Bacteremia is common after any dental procedures such as dental extraction, dental scaling and periodontal surgery [15]. The normal microbial flora helps in normal metabolism and vitamin production, whereas some microbes cause numerous oral diseases [16]. The normal microbial flora will cause the opportunistic infections. More consumption of carbohydrate-rich foods and industrially processed refined flour and sugar shifts the normal flora into a pathogen [17]. Continuous use of antibiotics converts the normal flora into an opportunistic pathogen which leads to a drug resistant microbe [18].

Also increased use of mobile phones may affect human oral microbes and leads to be pathogens. The continuous use of mobile phones increase the salivary flow rate and the volume of parotid gland and decrease the protein secretion [19, 20] which is the indicator of oxidative stress [21].

Diverse microbe in the form of biofilm causes dental plaque. The strong bond between microbes onto the tooth surface makes it difficult to treat the biofilm especially cells that forms the base of thickest biofilm [22].
1.1.3 ORAL INFECTIONS AND ORAL CANCER

The common oral diseases in humans are dental caries, periodontitis, root canal infections, alveolar osteitis and the interactions of microbes with host and environment [23]. The untreated oral infections may lead to many systemic diseases [24] in humans such as diabetes, heart diseases [25, 26], underweight due to pre-term birth [27] and pneumonia [28] and stroke [29]. Oral cavity possess many microbes [30] and distributed among teeth, saliva and tissues [31, 32]. Even though some of the normal floras are common among humans; it is still unclear about the existence of specific microbes in oral cavity particularly in diseased conditions. It may vary from one individual to other based on their dietary, health conditions and environmental factors [33, 34].

Oral infections are mostly caused by the bacteria and fungi which colonize in the tooth surfaces [35, 36]. The bacteria colonize along with food debris and saliva, form a sticky substance that strongly adheres to the teeth called plaque [37]. It leads to tooth decay if it is not removed on a routine basis. The microbes present in the oral cavity produces an enzyme called glycosyltransferases and forms a water-insoluble glucan complex from sucrose which leads to the biofilm formation [38]. The overall human health is affected due to oral health problems which lead to causes systemic infections. Meanwhile, there is a close association between chronic dental infection and general health, which indicates that dental treatment, has to be taken in earlier stages of infection. One of the important examples is edentulousness (loss of teeth) which causes malnutrition in elder people; prolonged dental infection also leads to stomach ulcers, infective endocarditis and infective arthritis. A systemic infection like leukemia causes oral ulcers [39].

According to Paster, 2001 about 280 bacterial species have been identified from human oral cavity among 50% of the bacterial species can be grown only in the anaerobic conditions [40].
Oral cancer affects lips, cheeks, tongue, hard and soft palate etc., [41]. It is the sixth most common cancer of mankind. Approximately two-third of oral cancer patients were from developing countries such as Eastern Europe, Latin America, Southeast Asia [42] and particularly India having the highest incidence of oral cancer for men and women in the ratio of 2:1 [43]. In the past, oral cancers are common among elderly males whereas at present many studies are reporting oral squamous cell carcinoma in young males with age less than 40 [44]. Oral cancer is a multi-step process involving many functional genes in cell cycle, apoptosis, growth regulators and DNA damage [45]. Common symptoms include swelling, lumps, rough spots around lips, gums leads to red patches in the mouth. Bleeding in mouth, numbness, pain around oral cavity difficult to swallow or chew and speak. Other symptoms include chronic sore throat, change in teeth structure and sudden weight loss etc [41].

According to Stoll, 2010 [46], oral cancer patients has dysfunctional p53 protein which leads to the loss of control in cell cycle check points results in uncontrolled cell growth. The treatment of oral cancer is usually a combination of chemotherapy, radiotherapy or surgery and combination of these in advanced conditions. Chemotherapeutic drugs such as Cisplatin and 5-Fluorouracil can be used by medical practitioners for the treatment of oral cancer [47]. The treatment causes more side effects [48] and poor survival rates of patients during their adverse health conditions [49]. Moreover 40% cancer patients did not respond to the above treatments [50].

1.2 TREATMENT

The dental treatment is very painful and more expensive. Moreover the synthetic antimicrobial drug provides a temporary solution furthermore leads to various side effects to the host like vomiting, diarrhea and tooth staining. Continuous administration of synthetic antimicrobial drugs leads to drug-resistant microbes as well as alters the oral and intestinal micro flora of the host [51].
Orthodontic appliances tend to create void places such as gaps between teeth and appliances that are prone to microbial invasion and bacterial colonization [52]. Patients with fixed orthodontic appliances are found to have more \textit{S. mutans} than non-orthodontic patients [53]. Chlorhexidine is an international drug used to treat at 0.2% concentration. However, it has been reported for the adverse side effects such as staining of teeth, dorsum of tongue, alteration of taste and supragingival calculus formation [54].

The pharmacological industries produce the potential antibiotics recently with the help of researchers even though drug resistance of the bacteria also increased in recent years [55]. It is necessary to find out alternative remedies for the oral diseases.

\subsection{1.2.1 HERBAL MEDICINES}

Medicinal plants are more suitable alternate drug as well as low cost with no side effects when compared to synthetic medicine. The herbal based oral care products are helped to prevent the toxicity and tooth staining caused by triclosan, cetylpyridinum chloride, chlorhexidine and amine fluorides [53, 56].

Around 50\% of the anti-cancer compounds screening by researchers are from plant origin [57] and some of the plant originated anti-cancer drugs were in use commercially [57] such as taxol, vincristine, podophyllotoxin and camptothecin.

In order to reduce side effects and expensive dental treatments, people have started to use medicinal plants in direct ways (chewing herbs) and indirect forms such as toothpastes and mouth washes [59, 60]. Herbs have the ability to prevent diseases and promote oral hygiene [61]. Many developing countries have been successfully introduced oral care medicinal plant products [62-64]. Herbal mouthwashes exhibit a great potential to treat plaques and it is an alternative for children and patients in need of special care [65]. It is a natural alternative for synthetic mouthwashes, gels, varnishes and chemicals which causes indigestion in children. Mouthwashes containing various herbs like pilu,
commonly called tooth brush tree, bahera (*Terminalia bellirica*), wintergreen oil, ela (cardamomum), peppermint satva (*Mentha piperita*) and yavani satva or ajwain (*Trachyspermum ammi*) are used to treat gingivitis [66]. Blending more than one herb in a mouthwash exhibits a great potential in improving oral hygiene and preventing dental carries and gingivitis via plaque control [67]. The major setback in using plant extracts is difficulty faced in extracting and characterizing the active molecules, time consumption and elaborate apparatus required [68].

1.3 HYPOTHESIS (MOTIVATION AND PROBLEM STATEMENT)

The selected medicinal plants *Glycyrrhiza glabra* (licorice), *Matricaria chamomilla* (chamomile), *Eclipta alba* (false daisy), *Morus alba* (mulberry), *Asparagus racemosus* (shatavari) and *Murraya koenigii* (curry leaves) possessing the anti-bacterial, anti-fungal against oral pathogens and oral cancer.

1.4 OBJECTIVES

1. Qualitative, quantitative estimation of phenols, flavonoids and antioxidant activity of selected medicinal plants.

2. Screening of *in vitro* antibacterial and antifungal activities and their mechanism of action towards human oral pathogens.

3. *In vitro* cytotoxic activity of crude plant extracts against oral cancer cell line.

4. Chemo - preventive potential of *Matricaria chamomilla* through 7, 12- Dimethylbenz (a) anthracene (DMBA) induced oral carcinoma in C57 black mice.

1.5 REVIEW OF LITERATURE

1.5.1 QUALITATIVE, QUANTITATIVE AND GC-MS ANALYSIS OF MEDICINAL PLANTS
The hydro methanolic extracts of *G. glabra* root were analyzed for the phytochemical constituents and anti bacterial activity against *Shigella flexneri*. The results indicated the presence of saponins, flavonoids, alkaloids, terpenoids and steroids in the phytochemical analysis and also possess high sensitivity towards the bacteria in the concentration of 80 µg/ml [69].

The successive extraction of *M. chamomilla* dried flowers with petroleum ether, ethyl acetate and methanol showed the presence of various phytochemicals like sterols, triterpenes, flavonoids, saponins, tannins and alkaloids [70].

The qualitative screening of phytochemicals were analyzed with ethanol, chloroform, benzene, petroleum ether and aqueous extracts of *E. alba* showed the presence of terpenoids in all extracts and flavonoids in ethanol, chloroform, aqueous extracts. Glycosides were present only in the ethanol extract [71].

The antioxidant potential of *G. glabra*, total phenols and flavonoids were estimated in the methanolic root extract. The total phenol and flavonoid content were quantified in the different solvents of *G. glabra*roots. The total phenol and flavonoid content were found to be 7.47 mg/gm GAE and 2.25µg/gm QE. The heavy metals, aflatoxins and other pesticides are also analyzed in the extract. There was no detection of any of the toxins proves that this can be incorporated in the pharmaceutical formulations. [72].

The phytochemicals were quantified in the *M. chamomilla* extracts by UPLC coupled with PDA detector method. The phenol content was 1.77 to 50.75 g of GAE/100 g and the flavonoid contents was 0.82 to 36.75 g QE/ 100 g [73].

The total phenol, flavonoid contents were determined in the *E. alba*ethanol extract. The phenol and flavonoid contents of the aqueous extract of *E. albawere found to be 0.5 mg GAE/g and 30.66 mg RE/g. the antioxidant
activity can also be influenced by the presence of phenols and flavonoids contents. [74].

The essential oils of *M. chamomilla* were analyzed for their chemical constituents. The obtained oil was blue in color and the yield was 0.9% (w/w). The major compounds present in *M. chamomilla* were P-cymene-8-ol, azulene, p-cymene, 1,8-cineole, artemisia alcohol, α- Elemene, cis- α -farnesene, trans- α - farnesene, borneol, α -Cadinene, spathulenol, α - eudesmol, α - bisabolol oxide B, α - bisabololoxide A, α - bisabolol, chamazulene and germacrene D were analyzed by GC-MS. The mild antibacterial activity of *M. chamomilla* oil was observed [75].

The presence of 2-propanone, 1, 3-dihydroxy-2-frunancarboxy aldehyde, 5-hydroxymethyl, hexadecanoic acid, n-hexadecanoic acid, 2 (octyloxy), 9- nonanediol were identified from the methanolic root extracts of *A. racemosus* by GC-MS analysis [76].

### 1.5.2 ANTIOXIDANT ACTIVITY OF MEDICINAL PLANTS

The essential oils of chamomile and fennel were analyzed for their antioxidant activity. The GC-MS analysis revealed that trans - anethole, estragole, fenchone and limonene were present in high amount in the samples tested. The highest radical scavenging activity was observed in the methanol extract of the essential oil of chamomile and the least activity was observed in the hexane extract of fennel [77].

Antioxidant activity of mulberry leaves were examined by DPPH assay and the bioactive compounds caffeoylquinic acids and flavonols were identified by GC-MS analysis [78].

The radical scavenging activity of the methanolic extract of *M. koenigii* was found to be 50.7% at the concentration of 100 µg/ml DPPH method. Benzene extract of *M. koenigii* showed the highest activity of 88.3% [79].

The effect of temperature and different solvent system on antioxidant property of plant was determined in *M. koenigii* leaf extracts. The combination
of ethanol and water in the ratio of 1:1 showed the maximum antioxidant activity of 100% at 10µg/ml concentration.

1.5.3 ANTIBACTERIAL ACTIVITY

The extracts of chamomile and fennel showed various levels of antimicrobial activities. The dose dependent responses were observed in both extracts. The least minimum inhibitory concentration was observed for Aspergillus flavus, Candida albicans, Bacillus cereus and Staphylococcus aureus [77].

The G. glabra showed an excellent response against oral pathogens in agar disc diffusion methods and also the MIC by broth dilution as well as agar dilution methods. The G. glabra showed a bactericidal activity of all the six human oral pathogens. According to the previous study by Fereshteh Sedighinia, 2012 the licorice plant can be used to treat dental infections since there was no resistance was observed during the study [80].

The antibacterial activity of methanol, ethanol and aqueous extracts of M. koenigii were determined against S. aureus, P. aeruginosa and C. albicans, of which methanol and ethanol extracts showed significant zone of inhibition against all the microbes tested. However aqueous extracts did not showed any activity [81].

The crude ethanolic leaf extract of M. alba were examined against the periodontal pathogens. Porphyromonas gingivalis was the most sensitive microbe with 1.95 mg/ml MIC value [82].

The antibacterial and antifungal activities of acetone extract of chamomile flowers were compared with the traditional treatments such as fucidic acid cream and placebo. The chamomile flower extract showed highest activity against the bacteria, S. aureus and C. albicans when compared to the traditional methods [83].
1.5.4 ANTI ADHERENCE ACTIVITY

The extracts of *Vitis vinifera* were active against the artificial biofilms contains various bacteria such as *Streptococcus mutans*, *Lactobacillus rhamnosus*, *Streptococcus sobrinus*, *Porphyromonas gingivalis* and *Fusobacterium nucleatum* [84].

The adherence of oral bacteria was reduced with cistus tea, red wine and grape juice up to 66% due to the presence of polyphenols [85].

1.5.5 SORBITOL ASSAY

The antifungal activity of a compound, 7-hydroxy-6-nitro-2H-1-benzopyran-2-one, a coumarin derivative was analyzed against *Aspergillus fumigatus*. The MIC value was increased 4-fold in presence of sorbitol which indicated that the target of Cou-No2 is the cell wall structure [86].

The antifungal activity of citral, commercial oil from citrus fruit was examined and its mechanism of action against *C. albicans* were also determined. The MIC and MFC were found to be 64 and 256 µg/ml respectively. The formation of conidia and hyphae were also inhibited. The target of action was not the cell wall or cell membrane which was confirmed by sorbitol and ergosterol assays [87].

1.5.6 MECHANISM OF ANTIFUNGAL ACTIVITY

The saponins from the root bark of *Dioscorea nipponica* were examined against the *C. albicans*. The membrane disruptive action of dioscin in *C. albicans* were demonstrated by flow cytometry reveals the decrease in cell size, morphological changes which further invading to cell membrane and causes the death of *Candida* were visualized by model membranes of rhodamine - labelled
giant unilamellar vesicles. The decrease in the size of fungal cells shows the antifungal activity of the dioscorea [88].

The antifungal activity of *Allium sativum* were tested against the skin invaded dermatophytes. The extract in the concentration of 2 and 4 mg/ml were found to be effective and the mechanism of antifungal activity was examined by electron microscopy. The fungal cells showed rough surface morphology in SEM breakdown of cell wall, cell membrane, disintegration of cytoplasm in TEM [89].

The ethanolic extract of whole fruit of pomegranate was tested against *C. albicans, C. krusei, C. rugosa*. The MIC was observed as 125 µg/ml. The vacuole formation, irregular hyphae were identified in the *C. albicans* treated with pomegranate extract by TEM [90].

**1.5.7 MTT ASSAY**

The pharmacological activity of methanol and aqueous extracts of *M. chamomilla* were analyzed. The major compound identified was apigenin07-O-glucoside. This compound is highly stable and has longer shelf-life. The methanol extract of *M. chamomilla* showed an excellent response to prostate and cervical adenocarcinoma, breast and colon carcinoma and fibrosarcoma cell lines. Apigenin and glucosides were majorly responsible for the inhibition through deconjugation of glycosides. Also the extraction process, storage conditions highly influence the biological activity through changes in pharmacological profile of chamomile flowers [91].

The anticancer activity of *M. koenigii* was investigated and the anticancer compound girinimbine, a carbazole alkaloid was active against A549 lung cancer cells. The isolated compound has an apoptotic activity with the IC<sub>50</sub> value of 19.01 µM. The apoptotic and antiapoptotic proteins from girinimbine possess anti-proliferative activity by their up and down regulation. The upregulation of p 53, p 21 and p27 were confirmed the apoptotic activity of the isolated compound [92].
1.5.8 MORPHOLOGICAL AND BIOCHEMICAL PARAMETERS

The bacoside A, a terpenoid, isolated from the chloroform and methanol mixture in the ratio of 2:1 were analyzed for the anticancer activity in the breast and colon cancer cell lines and in the in vivo mice model. The compound from the *Bacopamonnieirir* showed an excellent activity in the concentration of 200 and 500 mg/kg body weight of the mice. The body weight, tumor weight were significantly reduced in the tested animal shows the anti proliferative activity of the bacoside [93].

The anticancer activity of alcoholic and aqueous extract of *Barleriagrandiflora* leaf extract were tested in animal model against the lymphoma ascites and Vero cell line. The plant extract showed the activity at the concentration of 143.4, 210.8 µg/ml in lung cancer and lymphoma cell lines respectively. The tumor weight and volume were reversed to the normal level when compared to the control mice. Also the hematological parameters were reversed to the normal animal model [94].

The ethanol and aqueous extract of *Scaevolataccada* leaves were investigated for their anti cancer activity in Swiss albino mice. The phytochemical analysis confirms the presence of flavonoids, saponins, steroids and glycosides. The plant treated animal shows difference in the tumor weight and volume in the concentration of 200 and 400 mg/kg body weight. The biochemical markers SGOT, SGPT, ALP and restoration of antioxidant capacity were also well maintained. This confirms the anticancer activity of *S. taccada*. [95].

The acute and sub acute toxicity of the ethanol extract of *Pericampylusglaucus* leaves were investigated by giving high dose of extract (300, 2000 and 4000 mg/kg) for 72 hours and 600 and 1000 mg/kg for 28 days
respectively. The acute toxicity studies reveal that there are no mortality or biochemical changes but had slight drowsiness and lethargy. In contrast sub acute toxicity studies increase the activity of biochemical enzymes after 28 days. This study indicates the non toxic effect and the pharmacological activity of the plant extract [96].

1.5.9 ANTIOXIDANT ACTIVITY

The hydro alcoholic extract of *M. chamomilla* was investigated for paraquat (PQ) induced pulmonary injury and antioxidant activity. Paraquatin (dosage of 5mg/kg/day) and *M. chamomilla* (dosage of 50 mg/kg/day) were administered alone and in combination. The lung tissues were isolated and tested for the antioxidant activity. The extract werefound to be effective against oxidative damage in lungs of rats.*M. chamomilla* treated tissues showed the values of LPO, SOD and GPx near to the normal control groups confirmed the antioxidant potential of *M. chamomilla* [97].

The *in vitro* and *in vivo* antioxidant activity of aqueous extract of *Celosia argenteavarcristata* leaves were analyzed against oxidative stress induced by cadmium in the *Rattusnorvegicus* rats. The phytochemical analysis reveals the presence of various compounds such as cardiac glycosides, cardenolides, alkaloids and saponins. The tested plants show the antioxidant activity at the dosage of 400 mg/kg body weight. The cadmium induced oxidative stress was attenuated in the plant extract treated groups and concluded the scavenging activity [98].

The methanolic extract of *Solenaamplexicaulis* were tested for the antioxidant activity in CCl₄ induced hepatotoxic animal models. The various enzyme levels such as SGOT, SGPT, total bilirubin, total protein, ALP, CAT, GSH and LPO were near to the normal level in the
treated groups compared to the control group. The phenol and flavonoid 
present in the plants contribute to their antioxidant capacity [99].

The bioactive compounds from the ethanol extracts of *Melothria heterophylla* were 
isolated and identified by TLC and HPLC as gallic acid and rutin. The acute toxicity 
studies and antitumor activity were performed to check the toxicity and anti cancer 
activity. The results revealed that the isolated compounds possess no toxicity and active 
against EAC tumor bearing mice. The decreased levels of lipid per oxidation and also the 
increased levels of glutathione and antioxidant enzymes suggested the effectiveness of the 
plant against cancer [100].

**1.5.10 HISTOPATHOLOGY AND IHC MARKERS**

The novel anticancer agent, Pyrithione Zinc (PYZ) were identified from the six 
chemical library screening which consist of 5170 molecules. They are very 
effective in inhibiting the proliferation of oral cancer cells and inducing 
apoptosis. The histopathology of liver and kidney were performed with 
haematoxylin-eosin stain in the control and Pyrithione Zinc (PYZ) treated 
animals. There were no signs of necrosis or lesions in the treated group animals 
liver and kidney. The down regulation of various signaling pathways such as 
Cyclin D1 and Pyruvate kinase M2 were also identified [101].

The cell viability for the OSCC cell lines were assessed after the 
treatment with an antifungal agent Clotrimazole. The antifungal agent showed 
the increase in apoptosis in OSCC and down regulates Bcl-2 and up regulation 
of Bax. The above result indicates he arrest of cell cycle and induction of 
apoptosis in OSCC. There were no abnormalities in the heart, spleen, liver, 
kidney and gastrointestinal tract of the treated animal whereas the complete 
damage was observed in the control group which was confirmed by 
histopathology [102].
The *in vitro* anticancer activity against tongue carcinoma was investigated with the kuding tea. The kuding tea was found to active against cancer at the concentration of 200 µg/ml. The up regulation of Bax, Caspase-2 and Caspase-9 expression and down regulation of NF-κB, iNOS and COX-2 were observed in the Ilex Kudingcha tea treated animal model. The anti inflammatory activity and anti metastatic activity were also exhibited by matrix metallo proteases. The result indicates the buccal mucosa cancer preventing ability of the Ilex Kudingcha tea [103].

The expression of COX-2 in normal and oral lichen planus of OSCC patients were analyzed by IHC, RT-PCR and MMP expression. The COX-2 mRNA expression was significantly higher in the oral lichen planus (OLP) patients and absent in the normal oral mucosa shows that the COX-2 expression associate with the clinical stages of OSCC. The abnormal expression of COX-2 was observed during the advanced stages of oral cancer [104].

The COX-2 over expression in the chemotherapy patients can be used as prognostic marker. The size of tumor were compared with the expression of COX-2. Over expression of COX-2 were found in higher tumor size patients [105].

The biopsy tissues from the oral cancer patients were collected and it was immunohistochemically determined for the p 53 protein. The protein was over expressed in the malignant, pre-malignant and completely absent in the benign cases. A tumor suppressor gene, p53 can be considered as an important tool for the detection of oral cancer as it is over-expressed in OSCC [106].

A correlation between nitric oxide synthase and p53 were studied in the OSCC patients and it was correlated with the tumor stages. The expression and the clinical stages of cancer correlated with each other and it was confirmed by immunohistochemistry whereas there was no correlation between iNOS and p53. The results suggested that both are related with the tumor stages and lymph node metastasis, whereas there was no correlation between nitric oxide synthase and p53 [107].
Ki-67, non-histone protein located on chromosome 10q25 with a molecular weight of 345 to 395 KDa. It has important role in cell cycle regulation, ribosome synthesis and various neoplasms. It was expressed in all stages of cell cycle except in Go and early G1, increased in G2 and M phases. The Ki 67 detection in the oral cancer is also an accessible method [108].

The relationship among p53, Ki-67, C-erbB2 expression were compared in the oral leukoplakia diagnosis. A marked correlation observed between p53 and Ki-67 and both were increased in oral dysplasia. However only the cytoplasmic expression were observed in C-erbB2 indicate incomplete receptor degradation [109].

The expression of Ki-67 between well differentiated (WDSCC) and poorly differentiated (PDSCC) OSCC were observed to evaluate the grading of cancer. The results concluded that the over-expression of Ki-67 antigen was observed in well differentiated OSCC then in poorly differentiated OSCC [110].

The Ki-67 antigen can be used to detect the presence of oral cancer by the immunohistochemical staining. Ki-67 had a positive correlation with the histological grading of OSCC. The expression Ki-67 antigen increased with the stages of oral cancer [111].

1.6 CONCLUSION

Based on the collected literature, the selected plants possessed the various biological activities. The effect of the selected medicinal plants activity towards the oral pathogens and oral cancer has to be determined.