SUMMARY AND CONCLUSION

Oral squamous cell carcinoma, the sixth most common neoplasm of the head and neck region is a disease with high morbidity and mortality. There is substantial evidence demonstrating the role of reactive oxygen species and microorganisms in carcinogenesis. Hence antioxidants and antimicrobial agents can be beneficial to combat oxidative stress during carcinogenesis. Apoptosis and cell cycle dysregulation are the key features of oral squamous cell carcinoma. Hence anticancer agents that could induce apoptosis and cause cell cycle arrest would aid in treatment of the condition. Although surgery, chemotherapy and radiotherapy are the measures for management of the disease they are mutilating and accompanied by serious side effects such as nausea, vomiting, difficulty in swallowing and speech. Therefore, therapy to benefit cancer patients is still lacking. Recently, screening of herbs for antioxidant, antimicrobial and anticancer properties have been the subject of research for cancer management.

With this background, we have made an attempt to study the antioxidant potential, anticancer and antimicrobial effects of fenugreek seed (***Trigonella foenum-graecum* L.)**, cinnamon bark **(*Cinnamomum verum* J. Presl (bark)** and papaya leaf and seed **(*Carica papaya* L.)** extracts in oral squamous cell carcinoma cell line and on selected microbial strains**.** The anticancer effects of the standard cisplatin and the active compounds like trigonelline hydrochloride, cinnamaldehyde, 4 hydroxy cinnamic acid, eugenol, benzyl isothiocyanate of the extracts were also assessed.

The results of our study are summarised below:

- *Trigonella foenum-graecum* L. (seeds), *Cinnamomum verum* J. Presl (bark), *Carica papaya* L. (leaves of male and female plant) and *Carica papaya* L. (seeds) showed significant *in-vitro* antioxidant activity.

- *Trigonella foenum-graecum* L. (seeds), *Cinnamomum verum* J. Presl (bark), *Carica papaya* L. (leaves of male and female plant) and *Carica papaya* L. (seeds) exhibited mild antimicrobial activity against *Streptococcus mutans.*

- *Trigonella foenum-graecum* L. (seeds), *Cinnamomum verum* J. Presl (bark), *Carica papaya* L. (leaves of male and female plant) and *Carica papaya* L. (seeds) exhibited antimycotic activity against fluconazole resistant *Candida albicans.*

- *Cinnamomum verum* J. Presl. (bark), *Carica papaya* L. (leaves of male plant) exhibited anticancer effects via S phase arrest, induction of apoptosis and alteration of mitochondrial membrane potential). *Carica papaya* L. (leaves of female plant) and *Carica papaya* L. (seeds) exhibited anticancer effects via G2M and S phase arrest, induction of apoptosis and alteration of mitochondrial membrane potential. *Trigonella foenum-graecum* L. (seeds) exhibited very mild anticancer activity in oral squamous cell carcinoma cell line.

- The active compounds of *Trigonella foenum-graecum* L. (seeds)- trigonelline; *Cinnamomum verum* J. Presl (bark) - cinnamaldehyde, 4 hydroxy cinnamic acid and eugenol exhibited anticancer effect via S phase arrest, induction of apoptosis. Benzyl isothiocyanate of *Carica*

papaya L. (seeds) exhibited anticancer effect via induction of apoptosis by alteration of mitochondrial membrane potential.

- *Cinnamomum verum* J. Presl (bark) showed higher anticancer activity at a low IC_{50} concentration of 16µg/ml in comparison with the other extracts. The anticancer activity could be attributed to the active constituents like cinnamaldehyde, 4- hydroxy cinnamic acid, eugenol, polyphenols and tannins.

SUMMARY OF OUR RESULTS

Table 7.1: Summary of the antioxidant, antimicrobial, antimycotic and anticancer effects of *Trigonella foenum-graecum* L., *Cinnamomum verum* J. Presl and *Carica papaya* L.

Herb	Antioxidant Activity	Antimicrobial and antimycotic activity		Anticancer activity
		Streptococcus mutans	Fluconazole resistant *Candida albicans*	
Trigonella foenum-graecum L. (seed)	Present	Present (mild)	Present	S phase arrest.
Cinnamomum verum J. Presl, (bark)	Present	Present (mild)	Present	S phase arrest, induction of apoptosis by alteration of mitochondrial membrane potential
Carica papaya L. (leaves of male plant)	Present	Present (mild)	Present	S phase arrest, induction of apoptosis by alteration of mitochondrial membrane potential
Carica papaya L. (leaves of female plant)	Present	Present (mild)	Present	G2 M, S phase arrest, induction of apoptosis by alteration of mitochondrial membrane potential
Carica papaya L. (seeds)	Present	Present (mild)	Present	G2 M and S phase arrest, induction of apoptosis by alteration of mitochondrial membrane potential

Table 7.2: Summary of the anticancer effects of standard cisplatin and other phytochemicals present in the herbs

Active compound	Anticancer activity
Cisplatin	S phase arrest, induction of apoptosis by alteration of mitochondrial membrane potential
Trigonelline hydrochloride	S phase arrest, induction of apoptosis
Cinnamaldehyde	S phase arrest, induction of apoptosis
4 hydroxy Cinnamic acid	S phase arrest, induction of apoptosis
Eugenol	S phase arrest, induction of apoptosis
Benzyl isothiocyanate	Induction of apoptosis by alteration of mitochondrial membrane potential

With the above findings we conclude that,

1. The antioxidant property of the herbal extracts under study can be attributed to the presence of polyphenols and flavonoids which can be explored for oral cancer prevention and management.

2. The antimicrobial activity of the herbal extracts could be attributed to the presence of alkaloids, flavonoids, terpenes and polyphenols.

3. The anticancer activity of the herbal extracts could be attributed to the respective active compounds trigonelline of *Trigonella foenum- graecum* L. cinnamaldehyde, 4 hydroxy cinnamic acid, Eugenol, polyphenols, saponins, and tannins of *Cinnamomum verum* J. Presl, benzyl isothiocyanate of *Carica papaya* L.

This evidence emphasises on the importance of medicinal properties of plant extracts for oral cancer management, as herbal extracts are less likely to produce side effects since they have been a part of diet for several years.

FUTURE DIRECTIONS

1. Toxicity studies and *in-vivo* anticancer effects have to be evaluated.
2. A polyherbal formulation of the above mentioned herbs could be done for assessment of synergistic effect.

LIMITATIONS OF THE STUDY

The limitation of the study is that the study with an *in-vitro* design and preclinical trials, clinical trials and toxicity studies are yet to be carried out.

Figure 5.47: Schematic representation of the summary of results