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MEDICINAL PLANTS OF WEST MIDNAPORE, INDIA: EMPHASIS ON PHYTOCHEMICAL CONTAINMENT HAVING ROLE ON ORAL CANCER

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ABSTRACT

West Midnapore district, West Bengal of India is mostly covered with forests. A plant of these forests provides livelihood for the native people. The plantations are often conserved as sacred groves. The plants are utilized as source of foods, medicines and they are mostly involved in forest based product preparation and selling for their existence. They are mostly poor, uneducated and use local made tobacco product to reduce hunger which often causes oral cancer. The nature can fight with the situation. Precious natural molecules present in the plants of the forest as well as of the area can be judiciously used for the deadly disease itself. In this paper we have tried to search out those phytochemicals that can be obtained from the plants of this area and have previously documented chemopreventive and curative property on oral cancer may be due to the containment of many flavonoids, phenolic acids and carotenoids.

Key words: Carotenoids, Flavonoids, Herbal medicine, Phenolic acids.

INTRODUCTION

Oral cancer is one of the most common and deadliest diseases in all over the world. Sharp increase in the rate of oral cancer have been reported in several countries like France, Germany, Denmark, Scotland, USA, Australia, India, Japan, New Zealand, Central and Eastern Europe etc. According to a study of World Health Report published in 2005, the rate of oral cancer is 12.6 per 100,000 populations in India. It is seen that more male are affected than female (Peterson, 2009). In India 30-35% population is affected with oral cancer irrespective of rural or urban population (Ramya *et al*., 2011).

The major risk factors for the oral cancer are chewing betel-quid with or without tobacco, tobacco chewing and smoking, drinking alcohol etc. There are also few more risk factors like poor oral hygiene, bacterial and viral infection like Human Papiloma Virus infection etc (Chatterjee, 2009; Mork *et al*., 2001).

Few studies have shown that the risk of oral cancer can be reduced by the use of herbal medicine or phytochemicals as well as consumption of fruits and vegetables (Hsu *et al*., 2004, Liu, 2004). Many experiments have shown that this chemoprevention is attributed by the phytochemicals and herbal remedies due to having strong antioxidant and antiproliferative activities (Amin *et al*., 2009).

The herbal medication system is the oldest process which is passed on from centuries from generation to generation to cure diseases. Nowadays, due to the increasing use of herbal medicines and phytochemicals, there is immense need for increase in the cultivation of medicinal plants. Exploitation as well as conservation of natural plant resources must be therefore looked after in a proper way (Mitra and Banerjee, 2011).

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India is a place of natural diversity. In the state West Bengal, the southwestern districts like West Midnapore, Purulia, and Bankura etc are mostly covered by forest including different types of herbal plants. West Midnapore is mostly inhabited by the tribal populations as the industrial development has not still expanded in many areas of the place. In West Midnapore villages, most of the people are uneducated, and habituated to use medicinal plants for curing diseases (Ghosh, 2008). In the district some unique area comes under the tribal zone. Mainly the tribal like Santal, Munda, Bhumij, Koda, Mahali, Lodha, Kheria etc are inhabitant of the forests and conserve many plants as secret grove. They are involved with agriculture, cleansing of forest, digging works, pat art, bamboo art, stone and ornament work, clay statue, handloom and mat industry work etc. Along with that, these medicinal plants can be utilized to set up for small scale herbal industry here for development of this area (Bhakat and Sen, 2008). West Midnapore or Paschim Midnapore district is situated in the South Western side of the West Bengal, India. It is surrounded by Bankura district and Purulia district in the North, Balasore and Mayurbanj of Orissa in the South, Hoogly and Purba Midnapore in the East, and Singbhum of Jharkhand in the West. The geographical location is within 21°36 to 22°57 North latitude to 86° 33 to 88° 11 East longitudes. The district has four sub-divisions: Medinipur Sadar, Kharagpur, Ghatal and Jhargram.

West Midnapore district is characterized by a reddish ferruginous soil formed by the decomposition of the underlying rocks. The sandy loam of the reddish brown color that is mostly unproductive in nature covers the upper layer of the whole area. The parent rock is the metamorphic type rocks of sedimentary origin and igneous rocks both acidic and basic. The whole area is covered by many small forests. The total area of forest is 1,709 in Sq.Km including 8 Sq.Km reserved forest, 1,166 Sq.Km protected forest, 535 Sq.Km unclassed and other. Though these forests are conserved as sacred groves by the native peoples, still nowadays denudation of these forest lands is main cause of biodiversity endangerment (Ghosh, 2008).

In India Joint forest management takes a major role in improving lifestyle of rural people along with management of forest resource. A report suggests that 189 different non-timber forest products are used locally in Jamboni range of this area, out of 113 documented plant resources of this area, 27 are used for commercial purposes, 39 are consumed at home as food and 47 are used for medicinal purposes. In the food items, Sal (*Shorea robusta*) is used for smoking chutahs, and Kendu (*Diospyros melanoxylon)* leaves are used for preparing beedis. Both chutahs and beedis are types of local cigarettes. Mainly chewing of betel quid and smoking of these local cigarettes are the main cause of oral cancer in this area, about which the local uneducated people are quite unaware. So government takes the important roles about the awareness of cancer through modified district cancer control programme (Bhakat and Sen, 2008; Malhotra *et al*., 1993; Ray and Mandal, 2004).

Plants have been used from ancient time as a source of medicine. Nowadays herbal plants and ethno medicinal plants revived the importance in new area of medicine due to its low cost, ease of accessibility and lesser side effects. These are not only used for primary healthcare but also used in malignant diseases like oral cancer. Recent phytochemical and pharmacological examinations of plant extract have revealed a huge reservoir of bioactive compounds and epidemiological studies have shown that regular intake of fruits and vegetables may reduce the risk of chronic diseases such as cancer as they possess antioxidant capacity (Liu, 2004; Palombo, 2009). So public interest of herbal chemoprevention and treatment option is increasing steadily (Dey *et al*., 2010).

As previously stated that this area is mostly covered by forests, medicinal plants can be therefore exploited for herbal medicine. In this paper we have tried to find out those plants in West Midnapore area which contain phytochemicals having documented uses as well as possess chemoprevention property on oral cancer and other oral precancerous lesions.
Exhaustive list of plants and herbs grown in West Midnapore district was prepared through field survey of different areas. An extensive literature review was also performed to find out chemical components present in different part of those plants which have chemopreventive, or anti proliferative role on oral cancer and other precancerous lesions. In the table only those components have been tabulated which were documented only for above purpose.

Structure and brief account of natural chemopreventive compounds that prevent oral cancer

The plants, herbs, fungi, seeds are used as chemopreventive agents and medicines from time immemorial (Nobili *et al*., 2009).Chemoprevention, by definition is control of cancer by which the occurrence of the diseases can be completely demolished, slowed down or reversed by the administration of naturally occurring chemicals or synthetic agents (Amin *et al*., 2009). Recent studies have shown that mechanisms of chemopreventive potential may due to activity of anti-oxidants, induction of apoptosis, anti-inflammatory, anti-hormonal effect, immune enhancing effect, arrest on cell cycle and cell differentiation, suppression of proliferation and

angiogenesis as well as they have capacity to inhibit secondary modification and development of the neoplastic cells (Tsuda *et al*., 2004). Some of the natural compounds are listed below, which have ability to reduce the risk of oral cancer.

***Quercetin*:** Quercetin is a member of naturally occurring compounds flavonoids, which have documented protective effect against oral cancer. The structure of Quercetin in Fig.1 shows that it is a pentahydroxy flavonol. Like Catechin it has an identical number of hydroxyl group and contain 2, 3 double bond in the C ring and 4-oxo function (Catherine *et al*., 1996). Quercetin is widely distributed in the various plants and many of them are often consumed with fruits. It has the inhibitory effects on cell growth and morphological changes in SSC-9 oral cancer cell due to induction of apoptosis and necrosis (Haghiac and Walle, 2005).

***Kaempferol*:** Kaempferol has the almost same structure like Quercetin**,** but slightly differs in the B ring due to the absence of 3-hydroxyl group (Fig.2). This reduces the 27% antioxidants capacity of Kaempferol compared to Quercetin (Catherine *et al*., 1996). Like Quercetin, Kaempferol also has the anticancer capacity as it induces apoptosis in the various oral cancer cell lines (SCC-1483, SCC-25 and SCC-QLL1) (Kang *et al*., 2010).

***Curcumin*:** Curcumin is a yellow colored Phenolic pigment extracted from turmeric. It is immensely known for its anti – carcinogenic and other therapeutic activity. Curcumin has antitumor activity in oral cavity which can also inhibit cell growth and induce apoptosis in oral cancer cell. Recent study has shown reduction in cell viability of curcumin treated cells which can further induce apoptosis. Curcumin is also associated with down regulation of Notch-1 and nuclear factor κB (NF-κB) (Liao *et al*., 2011). Fig. 3 shows the structure of Curcumin.

***Catechin and Epicatechin*:** Catechin is a natural polyphenol antioxidant. It is also flavonoid in nature (Fig. 4). Catechin may be used as an anti oral cancer compound as it can inhibit the production of metalloproteases, reduces the invasion and migration and induces apoptosis. Catechin has evidence to prevent the growth of oral leukoplakia and oral cancer cell lines (Petty *et al*., 2009). Treatment with Epicatechin has been demonstrated for growth inhibition of oral squamous cell carcinoma cells too (Lee *et al*., 2004).

***Ferulic acid*:** Ferulic acid, chemically (3-methoxy, 4-hydroxy cinnamic acid) (Fig.5) is mostly present in grains, fruits and vegetables. It is derived from the metabolism of phenylalanine and tyrosine. Ferulic acid has anti-carcinogenic potential and pro-apoptotic effects on oral cancer cells. Researchers had shown the effect of Ferulic acid on expression pattern of apoptosis regulatory P53 protein and BCL-2 protein in oral squamous cell carcinoma (Balakrishnan *et al*., 2010).

***Caffeic acid*:** Caffeic acid is also a type of Phenolic acid found in fruits, grains and dietary supplements (Kang *et al*., 2009). Caffeic acid phenethyl ester (CAPE) synthesized from commercially available caffeic acid, have shown to exert cytotoxicity on oral submucous fibroblast (OSF), tongue squamous cell carcinoma (TSCC) cells and neck metastasis of Gingiva carcinoma (GNM). These results indicate that CAPE and its derivatives may have capability of chemoprevention against oral cancer (Lee *et al*., 2000). Fig.6 shows the structure of Caffeic acid.

***Naringin and Naringenin*:** Naringin and naringenin both are the flavonoids in nature (Fig 7a and 7 b). A study showed that naringin and naringenin have the inhibitory effects on DMBA induced oral carcinogenesis and both have the significant role in reducing the number of tumor cells (Miller *et al*., 2007).

***β-carotene*:** β-carotene is a naturally occurring compound belongs to carotenoids (Fig.9). Several clinical trials have shown that it can reverse the oral cancer formation and it has attractive chemoprevention property (Garewal, 1991).

***Lycopene*:** Lycopene is a carotenoid mainly found in tomatoes and other fruits and vegetables. The chemical structure of lycopene is almost same as β-carotene. The main difference is that the both end ring of lycopene is open (Agarwal and Rao, 2000).Experimental data suggest that lycopene can reduce the risk of the oral cancer as it have shown to inhibit the proliferation of KB-1 human oral tumor cell (Livny *et al*., 2002). Fig. shows the structure of Lycopene.

***Lutein*:** Lutein is a xanthophyll that belongs to Carotenoids family. It has two cyclic end groups including one alpha and one beta-ionone ring and the basic C40 isoprenoid structure (Fig. 11). It was shown that di-acetylated lutein has the antiproliferative activity on human mouth epithelial cancer KB cell line (Sun and Yao, 2007). Fig.17 shows the structure of Lutein.

***Gallic acid*:** Gallic is the one of the most biologically active phenolic compound and mainly found in plants in the form of free acid, esters, Catechin derivatives (Karmae, 2006; Chia, 2010). Gallic acid and its derivatives have anti-oxidant activity, anti-allergic, anti-inflammatory, anti-carcinogenic, anti-mutagenic, anti-neoplastic and apoptotic activities effects on oral

squamous carcinoma cells. Fig.13 shows the structure of Gallic acid.

***Ellagic acid*:** Ellagic acid (Fig. 19) has documented antiproliferative and antioxidant properties. It is present in various fruits, vegetables, nuts and berries including raspberries, strawberries, cranberries, blackberries etc. Ellagic acid has chemopreventive role in oral cancer. Ellagic acid may repress the growth of premalignant and malignant oral human cell line and also inhibit the 4-nitroquinoline-1-oxide (4-NQO)-induced tongue carcinogenesis in rat (Bisen PS *et al*., 2012).

***α-tocopherol*:** α-tocopherol is the branch of vitamin E (Fig. 15), which is referred to as a peroxyl radical scavengers and chain breaking anti-oxidants within the biological membrane. α-tocopherol has a phytyl tail with three chiral centers and an isoprenoid side chain (Meier *et al*., 2003). Extensive research has shown its anti-oxidant activity which also has evidence to prevent the development of cancers of the oral cavity in the animal model (Shklar and Schwartz, 1993).

***S-allylcysteine*:** Balasenthil S. *et al*. (2002) reported that s-allylcysteine have the chemopreventive effect in DMBA induced hamster buccal pouch carcinogenesis. In their experiment they revealed that tTG induction and repression of Bcl-2 expression is the cause of induction of apoptosis. Fig.16 shows the figure of s-allylcysteine.

***Ursolic acid*:** Subbaramaiah K *et al*. (2000) reported the chemopreventive mechanism of ursolic acid on oral leukoplakia cell line. They showed that ursolic acid may repress the induction of COX-2 by phorbol 12-myristate 13-acetate (PMA) in oral leukoplakia cell line too. Fig. 17 shows the structure of Ursolic acid.

Apigenin: Apigenin (Fig.18) is a type of flavonoid found in many fruits and vegetables. Apigenin has antioxidant, antimutagenic, and anticarcinogenic properties and have shown chemopreventive effects on DMBA induced hamster buccal pouch carcinogenesis (Silvan S *et al*., 2011).

***Luteolin*:** Luteolin (Fig.19) is a flavonoid. It has the antitumorigenic effects on oral squamous cell carcinoma. Researchers have shown that luteolin suppressed SCC-4 cell, a type of oral cancer cell and induced apoptosis by decreasing cyclins, anti apoptotic protein phosphorretinoblastoma (p-RB) cell dependent kinase (CDKs) (Yang *et al*., 2008).

***Aloe emodin*:** Aloe emodin (Fig.20) is a one type of phytochemical helps to inhibit the oral cancer. It is a natural anthraquinone which is found in some medicinal plants. Xio B *et al*., (2007) have showed that Aloe emodin may inhibit the KB cell lines of oral cancer.

Lupeol: Lupeol (Fig 21) is a triterpinoid found in the variety of plants, which has the ability to suppress the tumor growth. Lupeol can induce head and neck squamous cell carcinoma cell death (HNSCC) and damage this cell invasion by changing the action of NF-κB dependent epithelial to mesenchymal transition (Lee *et al*., 2007).

***Andrographolide*:** Andrographolide (Fig.22) is a very important bioactive compound mainly found in *Andrographis paniculata*. Wang L J *et al*. (2011) reported that andrographolide has the chemopreventive activity on DMBA induced hamster buccal pouch carcinoma by inhibition of NF-KB activation.

***Artonin E, Artobiloxanthone and Cycloartobiloxanthone*:** Artonin E, Artobiloxanthone and Cycloartobiloxanthone all three phytochemicals mainly found in the root of Artocarpus altilis. These are flavones in nature. Boonphong S. *et al*. (2007) showed that these compounds have cytotoxicity against KB cell lines of the human oral cancer. Fig.23 shows the structure of (a) Artonin E, (b) Artobiloxanthone, (c) Cycloartobiloxanthone.

***Folic acid*:** Folic acid (Fig.24), the member of vitamin B, is an essential constituent of the human and other animal's diet. Tetrahydrofolate, a reduced form of folic acid is oxidized to dihydrofolate or folate. The deficiency of folate may cause to increase risk of cancer in adults (Bonechi *et al*., 2004). So folic acid has immense chemopreventive properties. Folic acid is a water soluble vitamin, which has important role in cell proliferation and anti-tumor activity. It has been reported that folic acid receptor-targeted Dextran-Taxol-Folic acid (Dex-Txl-Fa) has shown the selective anti-tumor activity against human oral cancer cell line (KB) (Nakamura *et al*., 2011).

***Vitamin c or l-ascorbic acid*:** Vitamin C (Fig.25) is profoundly known for its anti-oxidant defense system. It works as a scavenger of free radical and blocks the harmful chain reaction triggered by the free radicals. Intake of vitamin C rich nutrients may lower the risk of oral cancer (Hegde *et al*., 2012). Vitamin C is also known as ascorbic acid. The unique features of vitamin C contain acidity without a carboxyl group, a stable γ-lactone ring, and two chiral carbon atoms (Arslantas *et al*., 2004).

Table: List of plants in west midnapore that has effects in oral cancer

Plant name	Local name	Scientific name	Family	Phytochemical related to oral cancer	References
Indian gooseberry	Amlaki	*Phyllanthus emblica.* (Syn.*Emblica officinalis*)	Euphorbiaceae.	Gallic acid, Ascorbic acid, Kaempferol, Quercetin.	(Baliga and Dsouza, 2011)
Indian lilac	Neem	*Azadirachta indica.*	Meliaceae	Vitamin C, Gallic acid, Catechin, Epicatechin.	(Biswas *et al*., 2002, Sabupriya, 2005)
Turmeric	Halud	*Curcuma longa*	Zingiberaceae.	Curcumin, α -tocopherol.	(Çıkrıkçı *et al*., 2008, Jurenka 2009)
White Marudah	Arjun	*Terminalia arjuna*	Combretaceae.	Ellagic acid.	(Amin *et al*., 2009)
Jackfruit	Katthal	*Artocarpus altili*	Moraceae.	Artonin E, Artobiloxanthone, Cycloartobiloxanthone.	(Boonphong *et al*., 2007)
Guava	Pearah	*Psidium guajava*	Myrtaceae	Lycopene.	(Amin *et al*., 2009)
Papaya	Pepe	*Carica papaya*.	Caricaceae	Vitamin C, Folic acid, Lycopene.	(Clinton 1998, Imaga *et al*., 2010)
pumpkin	Kumro	*Cucurbita maxima*	Cucurbitaceae	β-carotene, Lycopene, Lutein,	(Azizah *et al*., 2009, Bittar *et al*., 2010)
Tomato	Tometo	*Solanum lycopersicum*	Solanaceae	Lycopene, β-carotene, Lutein, Vitamin C.	(Ilahy *et al* 2011, Bhuvaneswari *et al*., 2004)
Lemon	Lebu	*Citrus limon*	Rutaceae	Ferulic acid,Caffeic acid, Naringin, Naringenin.	(Bocco, 1998, Miller *et al*., 2007)
Garlic	Rasun	*Allium sativum*	Amaryllidaceae	S-allylcysteine (SAC), Allicin.	(Tang *et al*., 2009 , Rahman, 2012)
Holi basil	Tulsi	*Ocimum sanctum*	Lamiaceae	Ascorbic acid, α-tocopherol, Ursolic acid, Apigenin, Luteolin.	(Nair *et al* 2009, Khare, 2008, Karthikeyan *et al*., 1999)
Aloe vera	Ghrita kumari	*Aloe barbadensis*	Xanthorrhoeaceae	Aloe emodin, Vitamin C, Vitamin E.	(Jain *et al*., 2011, Xiao *et al*., 2007)
Cabbage	Bandha kopi	*Brassica oleracea var. capitata*	Brassicaceae	Vitamin C, β-carotene, α-tocopherol, Lutein.	(Samec *et al*., 2011, Boyle *et al*., 1995)
Mango	Aam	*Mangifera indica*	Anacardiaceae	Lupeol.	(Amin *et al*., 2009)
Tamarind	Tentul	*Tamarindus indica*	Fabaceae	Luteolin.	(Amin *et al*., 2009)
The creat	Kalmegh	*Andrographis paniculata*	Acanthaceae	Andrographolide.	(Jarkamjorn and Nemato, 2008)
Spinach	Palang	*Spinacia oleracea*	Amaranthaceae	Luteolin.	(Amin *et al*., 2009)
Sweet potato	Ranga alu	*Ipomoea batatas*	Convolvulaceae	β-carotene.	(Sivakumar *et al*., 2010

Fig.1. Structure- Quercetin

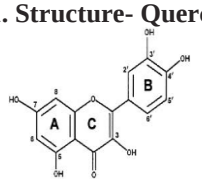


Fig.2. Structure- Kaempferol

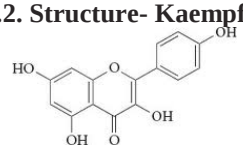


Fig.3 Structure-Curcumin

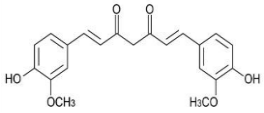


Fig 4. Structure- Catechin

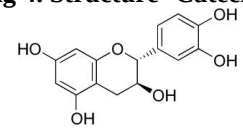


Fig 5.Structure-Ferulic acid

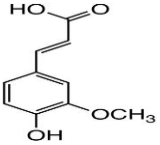


Fig.6.Structure-Caffeic acid

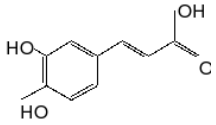


Fig. 7a Structure of Naringin

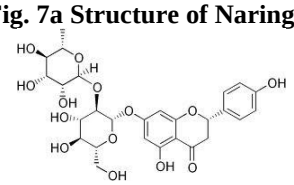


Fig.7. (b) Structure of Naringenin

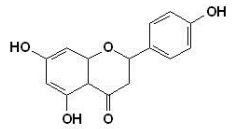


Figure 8 shows the biosynthetic pathway of some flavonoids and phenolic acids in plants

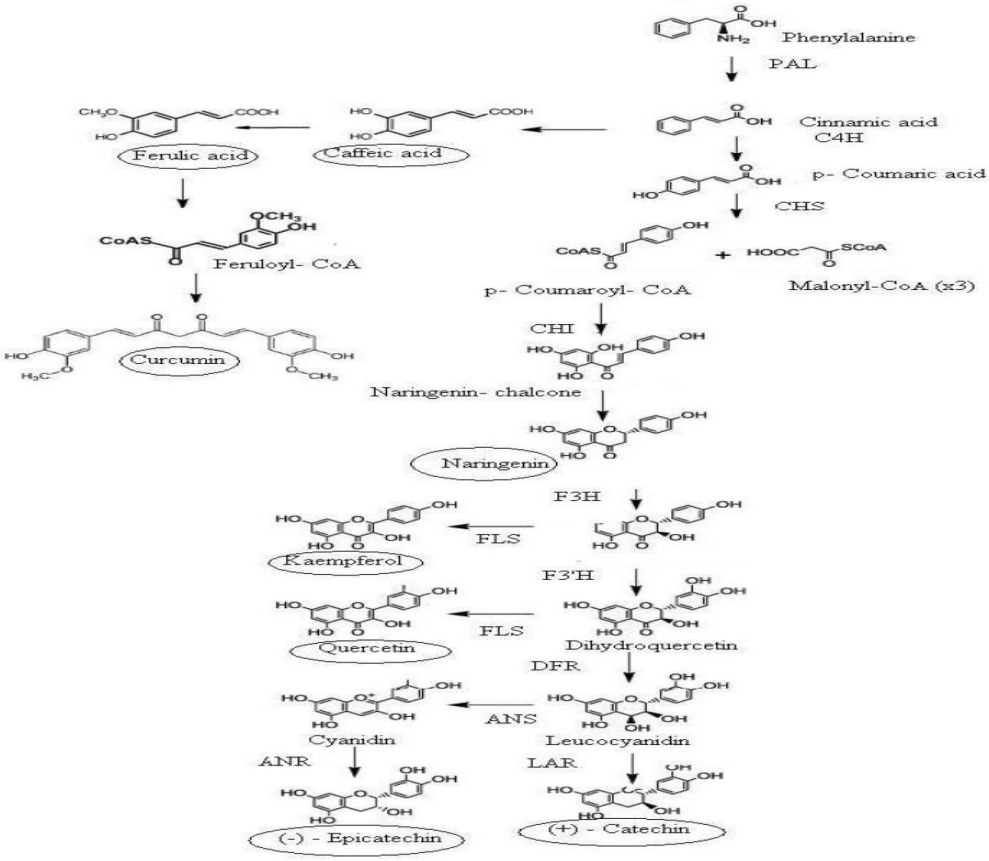


Fig.8. Biosynthetic pathway of Ferulic acid, Ceffeic acid, Curcumin, Naringenin, Kaempferol, Quercetin, Epicatechin and Catechin

Fig.9 Structure- β-carotene

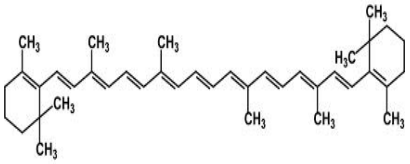


Fig.10 Structure-Lycopene

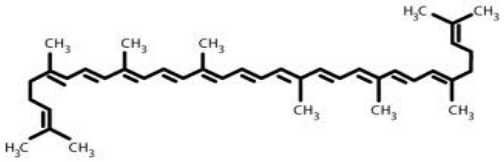


Fig.11. Structure-Lutein

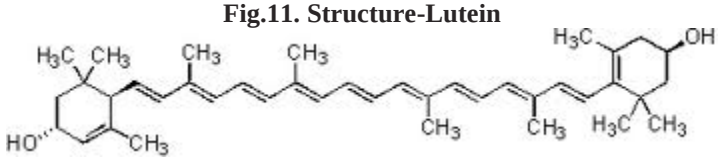


Figure 12 shows the biosynthetic pathway of some natural carotenoids.

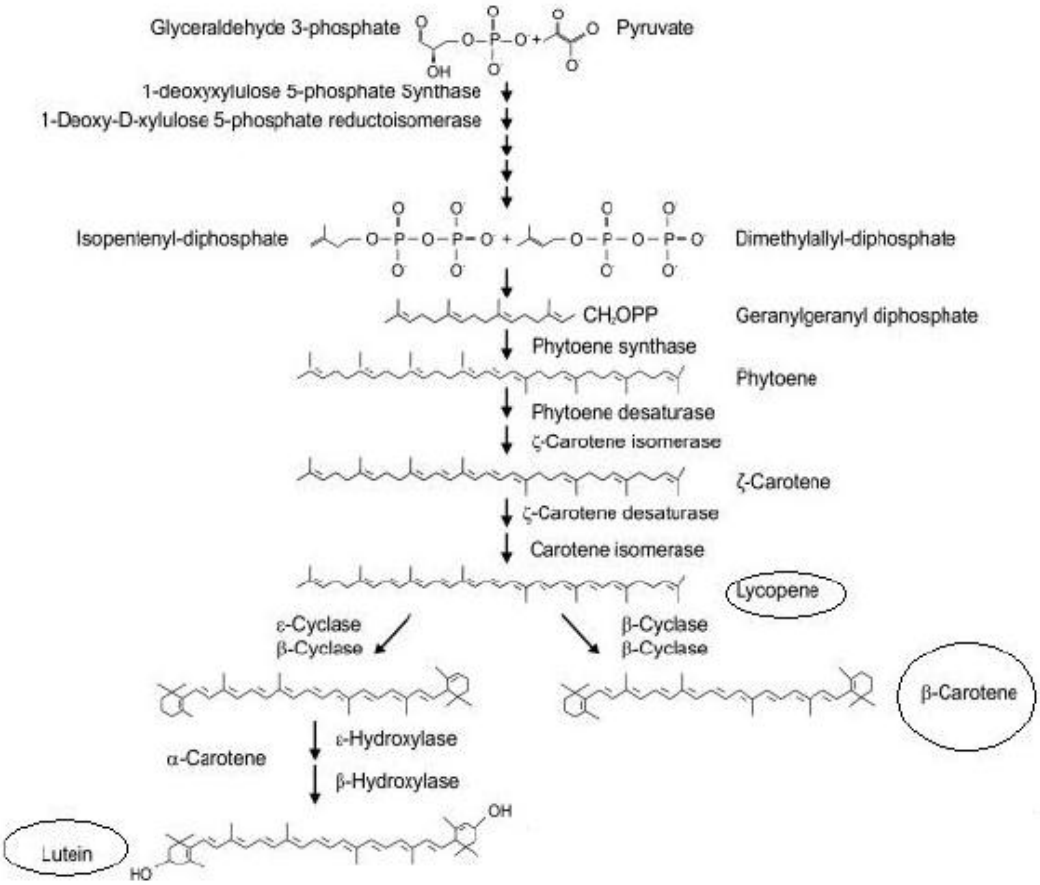


Fig.12. Biosynthetic pathway of Lycopene, Carotene and Lutein

Fig.13. Structure-Gallic acid

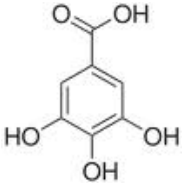


Fig.14.Structure-Ellagic acid

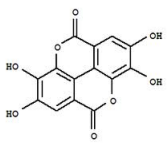


Fig.15. Structure- α-tocopherol

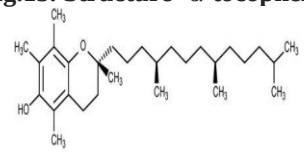


Fig.16. Structure - S-Allylcystiene

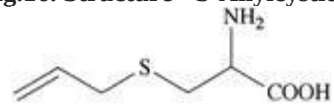


Fig.17. Structure-Ursolic acid

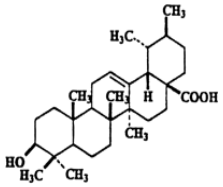


Fig.18. Structure-Apigenin

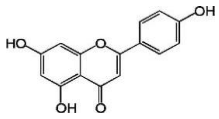


Fig.19.Structure-Luteolin

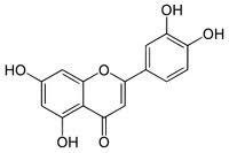


Fig.20. Structure-Aloe emodin

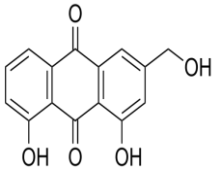


Fig.21. Structure-Lupeol

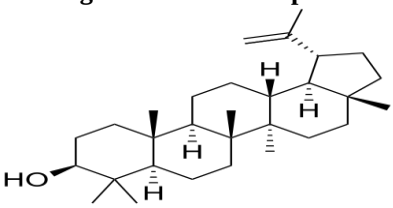


Fig.22. Structure-Andrographolide

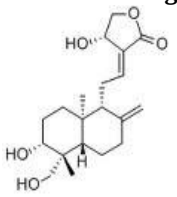
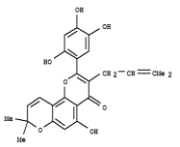
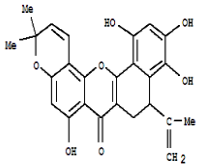


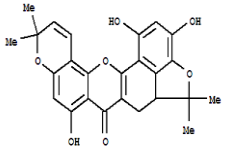
Fig.23 Structure- (a) Artonin E, (b) Artobiloxanthone, (c) Cycloartobiloxanthone.



(A)



(B)



(C)

Fig24.Structure-Folic acid

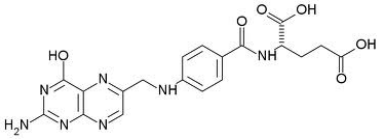
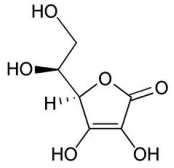


Fig.25. Structure-Vitamin C



CONCLUSION

From the field study to know about the local plants and extensive literature survey of components present in those plants, it is evident that West Midnapore District is copious with the natural resources of plants which contain many precious life saving molecules. If these medicinal plants can be exploited to set up small scale herbal medicine from the plant extracts, it will not only be economically beneficial for the native people, but will also be advantageous medically for the community for chemoprevention and cure of oral cancer. With the help of modernization of process parameters, and development in quality control, it is possible to utilize the natural potential for both medical and economical purposes of the area, West Midnapore.

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