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Effect of cigarette smoking on human health and promising remedy by mangroves

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ABSTRACT

This article reviews the evils of cigarette smoking and the promise of mangroves to cure them. Chemicals in cigarette smoke are leading cause of death to both smokers and non-smokers. Plant is the potential source to produce medicine for almost all the diseases. Mangroves are promising as a novel source of anti-cancer drugs in regulating the cancer pathways and stimulating immunity in the body system. Research on medicine from mangroves for the treatment of cancer has not only been shown to have an effect on cancer, but also provided important methods for the study of cancer therapy and mechanism. This report may help to explore the medicinal properties of the mangroves.

1. Introduction

Tobacco is regarded as “holy herb” and “God’s remedy”[1]. The genus *Nicotiana* belongs to the botanical family Solanaceae with characteristic viscid foliage and tubular flowers. There are more than 60 species of the genus, differentiated based on size and shape of leaves and flowers[2]. *Nicotiana tobacum* (*N. tobacum*) is an indigenous species to South America, while *N. rustica* to the West Indies. Nicotin is a volatile, colourless and oily liquid with poisonous alkaloid, which differentiates *Nicotiana* from other plants.

Tobacco causes human deaths, more than by all deaths from HIV, illegal drug use, alcohol use, and motor vehicle injuries, suicides, and murders combined[3]. Smokers die 14 years earlier than nonsmokers[4]. Tobacco smoking is a leading cause of human cancer and deaths which are higher in developing countries than in developed countries. About 70% of tobacco-related deaths will occur in developing countries[5]. About 1.3 billion smokers worldwide and half of them die due to smoking-related diseases[6]. About 13.3% of total deaths are expected in the year 2020 due to tobacco use[7]. About 50% of all smokers will be killed by use of tobacco[8]. Tobacco smoking is causing over 3 million deaths every year worldwide, and if current smoking trends continue the annual mortality will exceed 10 million by 2030[9].

Cigarette smoking, particularly beedis and chewing tobacco (smokeless use), is an age-old practice in India. However, the popularity of smoking among women and young children has increased recently many folds and is a significant public health problem[10]. In India alone, nearly 1 in 10 adolescents initiate tobacco use before 10 years of age. About 47% of the Indian males and 14% of the Indian females are tobacco users. Every year about 850000 new cancer cases are diagnosed, resulting in India about 580000 cancer related mortality[11]. Realising the seriousness of smoking, the present review has been prepared to analyze the status of issue.

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2. Toxic chemical composition of cigarette

Tobacco is grown and sold in many countries. The largest producers of tobacco are China, USA, the former Soviet States,

Brazil and India. Cigarettes are made from dried leaves of the tobacco plant. The chemical composition of tobacco varies widely with different sites due to the diversity of climatic conditions. Even within the same tobacco, the chemical composition of different leaves can be significantly different[12]. Chlorophyll a and b, neoxanthin, violaxanthin, lutein and β- carotene are also present in *N. tobacum*[13]. After the leaves of the tobacco plant are harvested and dried, they are treated with many chemicals. Cigarette smoke contains over 4 000 different chemicals and many of them cause cancer[14,15]. The cigarette smoke contains black sticky tar that contains toxic chemicals such as ammonia, toluene and acetone. Tar is the main cause of throat and lung cancer. It also causes the yellowish brown stains on fingers, teeth and lung tissue. Nicotine is the major drug found in tobacco which contributes to addiction to cigarette smoking which was first isolated from tobacco leaves as early as 1828[16]. Nicotine has a number of harmful effects on the human body in stimulating the nervous system, increasing heart beat, raising blood pressure and shrinking the small blood vessels under the skin shrink, which can cause wrinkles. Carbon monoxide is a poisonous gas that reduces the amount of oxygen taken up by red blood cells. Hydrogen cyanide damages the tiny hairs which act as natural lung cleaners of human bodies leading to accumulation of toxic substances in the lungs. The toxic heavy metals found in the cigarette smoke are: lead, nickel, arsenic and cadmium. Cancer-causing radioactive compounds are also found in cigarettes. Pesticides like DDT and methoprene do present in tobacco smoke which is used during tobacco cultivation. Other chemicals such as benzene, creosote, and some asphalts cause skin cancer, lung cancer and reduction in reproductive capacity. Among the 2 256 different smoke components, 542 find place in conventional smoke by a cigarette[17]. The highly carcinogenic compounds such as dimethylbenz(a)anthracene, dimethylnitrosamine and methylnaphthalene are added when the cigarettes are being made[18].

2.1. Cigarette smoking and cancer

Cancer-related death was estimated at 100 million in 20th century and is 1 billion in 21st century[19]. Cancer prevalence in the United States is about 300 cases per 100 000 populations, whereas that in Asian countries is less than 100 cases per 100 000 due to tobacco smoke[20]. It is estimated that in 2015, tobacco is projected to kill 50% more people than HIV/AIDS and will be responsible for 10% of all deaths globally[21]. Over 3 000 teenagers light up the cigarette for the first time every day[22]. In India, the International Agency for Research on Cancer estimated that about 635 000 people died from cancer in 2008, representing about 8% of all estimated global cancer deaths and about 6% of all deaths in India[23]. The temperature estimated at glowing tip of lighted cigarette burning is 800 °C. A smoker with each puff draws into his mouth and lungs, a hot collection of gases and many toxic particles[24]. Tobacco smoke may lead to changes in the lung tissue shortly after exposure, so called precancerous changes. Tobacco-related cancers represent 11.45% male cancer deaths and there were twice as many deaths from oral cancers as lung cancers in India[25]. Most of the lung cancer and emphysema, as well as a high percentage of heart attacks are caused by cigarette smoking[26].

Lung cancer is an aggressive and heterogeneous disease and most common malignant tumours worldwide[27-31]. The lungs are the most important organs that help us breathe and give oxygen to all the cells in the body. These organs affect directly or indirectly by cigarette smoking. Like all cancers, lung cancer cells have the ability to invade neighboring tissues and spread to distant parts of the body. It is usually classified as non-small cell lung cancer, which accounts for more than 80% of lung cancers and it is the most common cause of cancer deaths worldwide[32,33]. In women, lung cancer is the third-most common cancer worldwide, after breast and colorectal cancers[34]. Smokers are 5-10 times likely to develop lung cancer, about 87% of lung cancer cases are caused by cigarette smoking[35]. Every year, one million smokers die of lung cancer in USA, accounting for 25% of total smoking-related deaths (Figure 1). One in 10 moderate smokers and one in 5 heavy smokers (15 cigarettes per day) will die of lung cancer. About 85% of smokers with lung cancer die within 5.5 years. Many types of cancers including pancreatic cancer and colon cancer, bladder and kidney cancer are caused due to tobacco smoking[37]. Tobacco smoking is also associated with cancer of the oral cavity (including lip and tongue) in both men and women. Cigarette smoking causes not only lung cancer, but also cancer in urinary tract, oral cavity, oropharynx and hypopharynx, oesophagus, larynx, pancreas, stomach, cervix, leukaemia, female breast and prostate[38].

2.2. Cigarette smoking and human reproduction

Cigarette smoking affects adversely human fertility[39]. Chemical agents may affect male reproduction by means of direct effect on the testicular function and spermatogenesis. The mechanisms involve the hormonal control of spermatogenesis or through direct effect upon the germ cells and sertoli cells of the seminiferous epithelium. Such alterations in the spermatogenetic capacity in the male may lead to infertility or production of mutated spermatozoa which may subsequently cause poor pregnancy if the mutated spermatozoa are to fertilize an egg. Cigarette smoking causes different negative effects on human reproductive process such as abnormal sperm morphology, less motile sperm, smaller quantity of sperm, lower proportion of normally shaped sperm and changes in the number and arrangement of the microtubules of the sperm in a smoker as compared to a non smoker group of men[40-44].

Women are likely to have menstrual irregularities, infertility problems, cramps and hot flashes during menopause due to smoking. Smoking lowers the level of estrogen and attains early menopause with increased risk of osteoporosis and fractures[45].

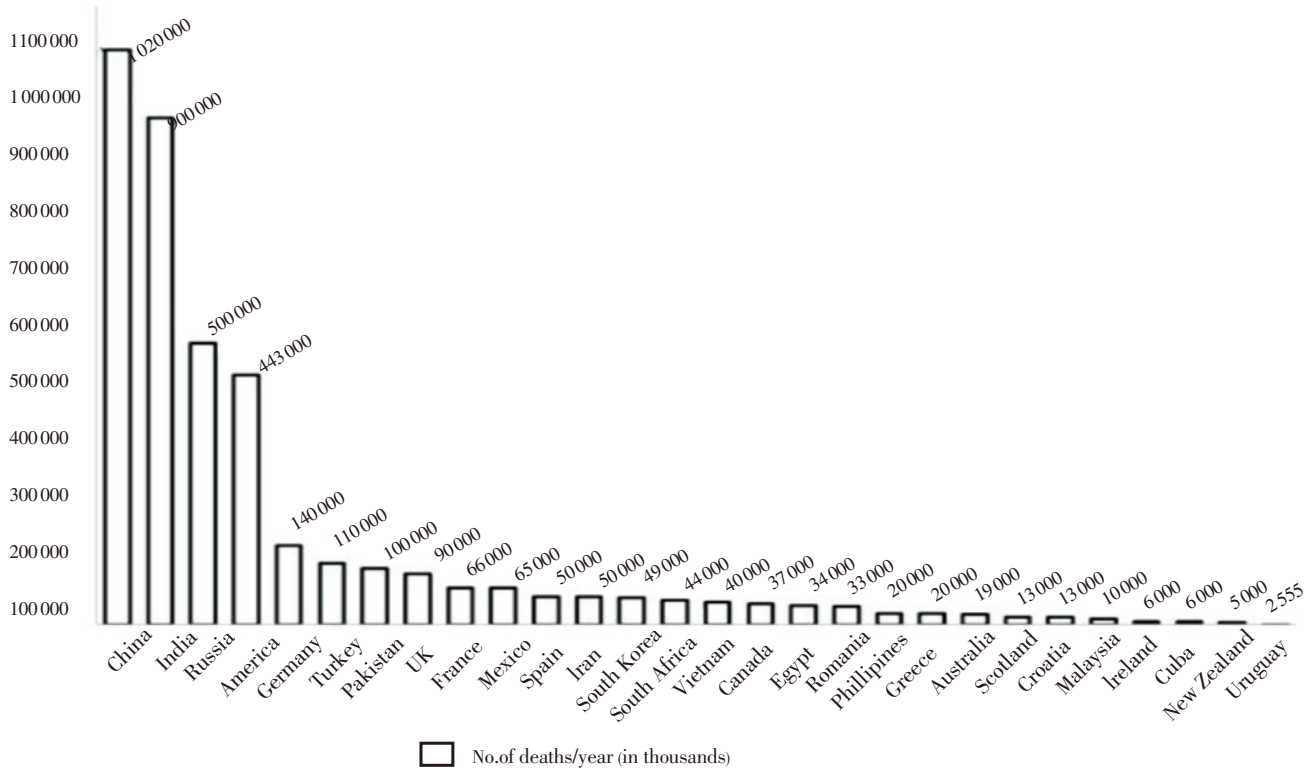

Figure 1. Annual global death due to cigarette smoking related diseases.

Cigarette smoking can interfere with almost every aspect of egg production, fertilization process, embryo attachment, growth and development of the baby during the pregnancy. From the initial step of woman pregnancy, cigarette smoking causes a number of problems such as deleterious effects on embryo transport, control of oocyte production, embryo viability, onset of menopause and bone metabolism. The smoke affects both the mother and the growing young ones. The smoke adversely affects both the humoral and cellular immune systems. Such alterations might affect epithelial response to inflammation result in an increased frequency of tubal infection and subsequent infertility. Possible early or deferred entry of blastocyst into the uterus and alterations in the immune system that can account for the smoking and decreased fecundity[46,47]. Exposure to cigarette smoke during pregnancy is associated with low birth weight, premature delivery, early pregnancy loss, prenatal mortality, and ectopic pregnancy[48].

2.3. Other harmful effects of cigarette smoking

Cigarette smoking contributes to remarkable risk factors of non-communicable diseases, including coronary heart disease, stroke, chronic obstructive pulmonary disease, peripheral vascular disease, peptic ulcer disease and tuberculosis[49]. Cigarette smoking is strongly associated with lung cancer, emphysema, chronic bronchitis, cardiovascular disease, and other serious internal diseases and cancers[50-54]. The non-stop chronic inhalation of cigarette smoke alters a wide range of immunological functions, including innate and adaptive immune responses[55].

3. Environmental impact of cigarette smoking

Smoking of cigarettes causes a great concern of environmental problems[56]. In the past 25 years, 52 907 756 cigarette butts have been collected from international beaches, accounting for 32% of all debris collected. The number of cigarette butts collected is over three times more than that of other wastage[57]. These butts may then be carried as runoff to drains, making their way to rivers and ultimately to oceans. Though the waste materials are biodegradable, it will take a long time of nine months to degrade the cellulose acetate and plastic materials present in the cigarette waste in the sewage water[58-60]. The studies conducted in the aquatic ecosystems have reported that the nicotinic acid and ethyl phenol present in the cigarette butts affect the fish and microbial communities[61-63]. Cigarette smoking releases about 2.6 billion kilograms of carbon dioxide in the air every year and about 5.2 billion kilograms of methane annually worldwide[64,65].

4. Mangroves in cancer treatment

The plant kingdom is potentially a very diverse source of chemical constituents with many bioactivity notably tumour cytotoxic activity. India has the richest source of medicinal plants among the world. About 25 000 effective plant derived drugs are used in folk medicine in India. There are 7 800 drug manufacturing units, which exploit about 2 000 tonnes of herbal plants every year in the country[66]. Natural products have played a significant role in drug discovery and development, especially as agents active against cancer and infectious diseases[67]. Several anticancer agents including taxol, vinblas-tine, vincristine,

camptothecin derivatives, topotecan and irinotecan and etoposide are in clinical use all over the world[68].

Traditional uses of mangroves recently attracted the scientific communities to find out the pharmaceutical products to combat a number of serious diseases[69]. Mangrove plants such as *Avicennia africana*, *Avicennia nitida*, *Bruguiera exaristate*, *Buddleja parviflora* and *Bruguiera sexangula* (*B. sexangula*) and some of the mangrove associates are also used to cure the cancer diseases by the fishermen communities[70,71]. The mangrove plants and their associates possess a strong antioxidant activity as they grow in the stressful environment conditions. *Excoecaria agallocha, Avicennia alba*, *Aegiceras corniculatum*, *Bruguiera gymnorrhiza*, *Ceriops decandra* (*C. decandra*), *Rhizophora mucronata*, *Rhizophora apiculata*, *Rhizophora stylosa*, *Sonneratia apetala*, *Acanthus ilicifolius*, *Ipomea pes-caprae*, *Sesuvium portulacastrum*, *Suaeda maritima*, *Heritiera fomes*, *Terminalia catappa* and *Pandanus odoratissimu* possess the free radical scavenging and antioxidant activity[72-78]. Mangrove plants are a rich source of steroids, triterpenes, saponins, flavonoids, alkaloids and tannins[79]. Natural products with antitumour properties can be classified into 13 distinct chemical groups such as alkaloids, phenylpropanoids, terpenoids, aldehydes, glycosides, lignans, lipids, unsaponified lipids, nucleic acids, polysaccharides, proteins and unidentified compounds[80].

About 32 plants, *Acanthus ebracteatus*, *Acanthus illicifolius*, *Acrostichum aureum*, *Avicennia alba*, *Avicennia marina*, *Barringtonia asiatica*, *Bruguiera cylindrica*, *Bruguiera gymnorrhiza*, *Buddleja parviflora, B. sexangula, C. decandra, Ceriops tagal*, *Cissus carnosa*, *Cordia cochinchinensis*, *Cynometra ramiflora*, *Derris trifoliata*, *Flagellaria indica*, *Lumnitzera racemosa*, *Nypa fruticans*, *Phoenix paludosa*, *Rhizophora apiculata*, *Rhizophora mucronata*, *Sarcolobus globosus*, *Sonneratia alba*, *Sonneratia caseolaris*, *Sonneratia ovata*, *Stenochlaena palustris*, *Suaeda maritima*, *Trianthema decandra*, *Weddelia biflora*, *Xylocarpus granatum* and *Xylocarpus rumphii* exhibit the antioxidant and cancer chemoprevention activity[81]. In the year of 2011, Kathiresan and his research team have proved anti-oral cancer effect of black tea extracted from the mangrove plant *C. decandra*[80]. Extracts of *B. sexangula* bark are active against two tumours, sarcoma 180 and Lewis lung carcinoma[82]. Twelve naphthoquinones isolated from the mangrove *Avicennia marina* exhibit strong anti-proliferative activities against L-929 mouse fibroblasts and K562 human chronic myeloid leukemia cell lines[83]. *Xylocarpus granatum*, *Aegiceras corniculatum*, *Calophyllum inophyllum* and *Excoecaria agallocha* display the strong anti-proliferative effect[84].

5. Conclusions

It is matter of necessity to develop potent drugs to treat smoking related diseases. It is a matter of urgency to consider effective way for prevention of smoke-related cancers. In this regard, plant bioactive compounds are important in the treatment of cancers. Natural products comprise of 14 out of the top 35 drugs on worldwide sales[85]. There are more than 270000 higher plants existing on this planet including mangroves but only a small portion has been explored scientifically. So, it is anticipated that plants can provide potential bioactive compounds for the development of new "leads" to combat cancer diseases. Finding remedy from natural sources is the only effective way to reduce the cancer diseases. In this regard, mangroves are promising as a source of medicines. Further research is warranted to develop potent drugs from the mangroves for smoking-related diseases in the following lines.

Broad based screening of mangrove species extracted in different solvents of various polarities against carcinogenesis; isolation, purification and identification of anti-cancer chemicals present in the potent extract; physical, chemical and biological characterizations of the bioactive compounds; formulation of mangrove-based drugs and testing their efficacy with standard drugs under *in vitro* and *in vivo* conditions; cost-benefits analysis for developing commercial ventures.

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