

## Plant extracts a potential anticancer tool

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**Abstract:** Investigations have been carried out at assessing the effects of arecanut extract against a battery of human and veterinary isolates. The aqueous extract of *Areca catechu* L was found to be inhibiting the growth and propagation of several bacteria, avian viruses and fungi including *Streptococcus mutans* an oral dental pathogen, New castle Disease virus and *Candida albicans*. The antioxidant studies of plant extracts namely arecanut extract showed positive results. The results are sufficient by itself to validate the use of several plant extracts to scavenge free radicals thus promoting and supplementing anticancer therapy. Arecanut extract was seen to be effective in reducing inflammation induced in mice by oedematogenic agents like dextran, carageenan and formalin. Arecanut extract was able to prevent the initiation of tissue injury seen in gastric mucosa and subsequent gastric ulceration. Oral administration of plant extracts like arecanut provided gastric cytoprotection. *Areca catechu* L has been seen to be of value in the management of male sexual disorders and studies were documented to establish aphrodisiac potential of plant extract. The whole chapter provides scientific rationale for the traditional use of plants in ameliorating the suffering of cancer patients and offers an adjuvant role in anticancer therapy by supplementing the existing treatment regimen in combating Cancer.

**Keywords:** Arecanut extract, antimicrobial, antioxidant, anti inflammatory, antiulcerogenic, aphrodisiac, turmeric.

## Introduction

Ayurveda, the science of life is a comprehensive medical system that has been the traditional system of health care in India for more than 5000 years. A number of plants could be useful in the present context to fight corona virus disease- 2019 caused by SARS-COV-2. The WHO has declared it as pandemic. Here we based on scientific evidence tried to use plant extracts against cancer or rather the use of plant extracts in ameliorating the side effects of Cancer therapy be it Chemotherapy and trying to either supplement it as effective tool to combat cancer along with Chemotherapy or radiation therapy treatment modality.

Many plants like Neem : *Azadirachta indica* or *Melia azadirachta* as leaves crushed in external application in skin disease, Greater cardamom: *Amomum subulatum* as seeds prescribed for the treatment of indigestion, vomiting, abdominal pain., Leaves of *Gymnema sylvestre* common name: Australian cow plant and Periploca of the woods, Hindi term Gurmar are given to diabetic patients., Arecanut palm nuts ( Arecanut): *Areca catechu* are prescribed in diarrhoea and urinary disorder as powdered nuts.

Arecanut has shown significant antiviral activity against human immuno deficiency virus( HIV). Arecanut extract may be explored as a potential anti covid treatment regime agent.

However drug induced toxic hepatitis or liver injury( DILI) is seen in diabetic persons on being treated with *Gymnema sylvestre*. Knowing pros and cons, we make an attempt to study the potential use of aqueous arecanut extract( AE) in treatment of cancer.

Cancer is a major problem that has plagued not just the developed countries like the United States but also developing countries like India. Developed countries have the rich economic back up to increase the mortality of its population and to ameliorate the suffering of cancer patients.. Developing countries like India on the other hand, with its diverse agricultural yield per hectare should possibly capitalise and exploit its agricultural resources.

Arecanut plays an important role in the social, cultural and economic activities of the people. India is the largest producer of arecanut in the world. The productivity of arecanut has increased from 845 kg/ha to 1243 kg/ha, now in the 21 st century. Kerala as a statistic study reveals has produced 84.7 tonnes of arecanut over an area of 93.2 hectares.



Arecanut is non toxic by itself. Arecanut and arecoline may inhibit the growth of oral mucosal fibroblasts and keratinocytes. The potential of such medication in reducing the cancer induced complication is enormous and if a therapeutic drug is developed it will be of great help in the cancer therapy. It would be an economic boon to the nations infrastructure. The possibility of a drug in cancer treatment or even an agent to relieve the suffering of cancer patients is a great contribution to humanity.

**Background of Use:** Because of its ancient history, its use is **socially acceptable** among all sections of society including woman and quite often children. Arecanut usually incorporated in betel quid is the fourth most common psychoactive substance in the world after caffeine, alcohol and nicotine..its use extending to several hundred million people. There are many types of ingredients and ways of preparing betel quid. There are several forms of arecanut: green unripe; ripe but raw; baked roasted or boiled; fermented; or processed with sweeteners and flavours, betel leaf ( or inflorescence) and ingredients consisting of spices, condiments, tobacco and lime. In India the most common way to use it is to use half a large leaf . 1 medium or 2 small sized betel leaves, smear them with slaked lime and a small amount of catechin containing substance (*catechu*, *gambir* or *kath*, but not in the southern region) along with pieces of arecanut . Only ripe arecanut is used generally after curing (roasting or boiling in water). Betel quid can be prepared plain (or astringent) or sweet . Sometimes Cardamom and often tobacco are added to the plain variety . In the sweet variety , cardamom , cloves, coconut, sugar crystals, camphor, amber, nutmeg, mace and even colouring agents are commonly added. In North eastern parts of India, fermented arecanut called 'Tamal' is frequently used.

**Significance:** After a quarter century of rapid advances cancer research has generated a rich and complex body of knowledge revealing cancer to be a disease involving dynamic changes in the system, be it physiological or genetic with an array of clinical manifestations. In par is the research and economic market advances towards developing anti cancer agents, drugs and diagnostic kits. In this light Arecanut has a significant quantity of phenols including catechin which has been shown to be useful in conditions of connective tissue disease. Moreover it is a good antioxidant. Free radical scavenging of arecanut extract , is a potential parameter for rating the value of an anticancer agent.

Anti metastatic activity of arecanut extract is a potential tool for studying and treating secondary cancer. Anti-inflammatory activity of arecanut extract is useful for secondary complications associated with cancer and HIV. Antimicrobial and antiviral activity of arecanut extract is useful for controlling bacterial and viral diseases. Controlling bacteria that causes dental caries , namely *Streptococcus mutans*, would be a contribution to Medical Microbiology , among the other broad spectrum activity of the agent against Gram positive and Gram negative bacteria. Anti diabetic activity , if it comes across as positive in animal studies and human trials , would be a milestone achieved in the treatment of Hyperglycaemia or diabetes, which has been a major disease that has affected even the juvenile section of the mass population.

### **Antimicrobial activity of plant extract namely aqueous Arecanut extract:**

The investigations for this study carried out reveals that aqueous extract of Areca catechu L was found to be effective for inhibiting the growth and propagation of several gram positive human isolates and gram negative veterinary and human isolates. It was found to inhibit the growth and propagation of *Streptococcus mutans* , the causative bacteria of dental caries.

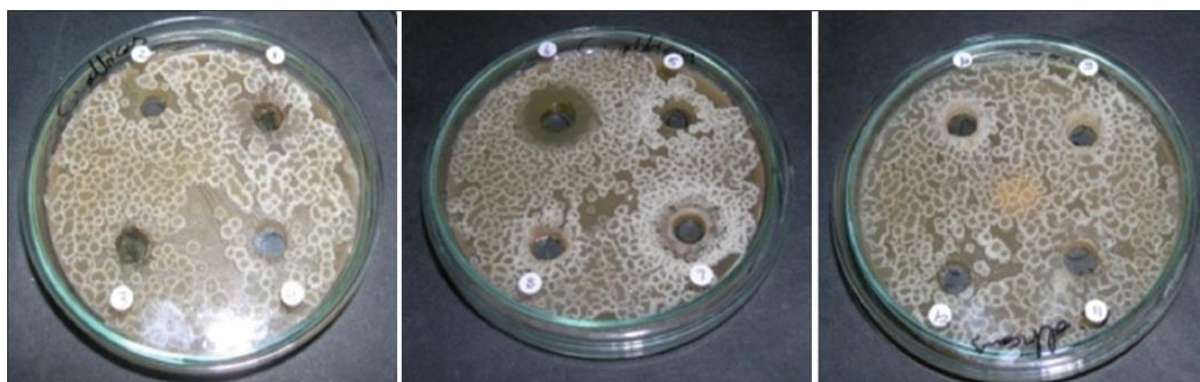
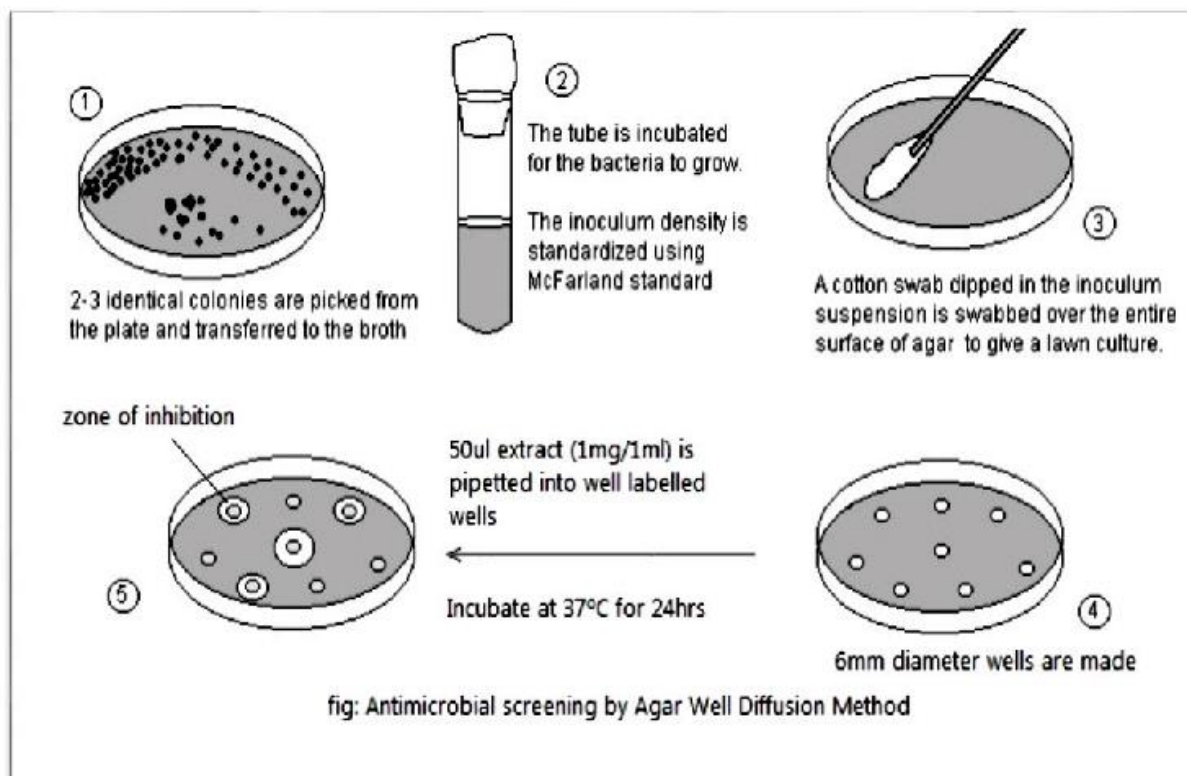
The envisaged use of arecanut extract as an antiviral agent against avian viruses such as New castle Disease virus and Egg Drop Syndrome Virus is also a subject of interest.. Determination of haemagglutination titres is the index of the amount of virus present in the allantoic cavity of the embryonated chick egg at the end of five days. The results indicate the concentration dependant reduction of the virus in the allantoic fluid . There was a need of further investigations to be carried out to support the antiviral activity of arecanut extract . In fact Arecanut has been shown to inhibit replication of HIV.

Since the present Covid pandemic caused millions of deaths world-wide, scientists and other drug making companies are looking forward to discover the vaccine against corona virus. Corona virus, respiratory disease, also leads to the death can be compared with the Influenza virus due to its hazardous nature. Influenza can be considered as the never-ending threat to the humankind. Plant extracts are cheapest source with lots of antimicrobial activities reported. As we can see the symptoms of the both Influenza and corona which starts with the respiratory

problems, followed by fever and flu, we could envisage a study to treat both the viruses with the same arecanut extract. Since areca nut extract is reported with high percentage of anti-microbial activity, and there is no similar works have been done, we hope that an attempt could lead to success, and the possibility that one may be able to develop economically reliable, efficient, cost-effective remedy for the corona virus disease 19.

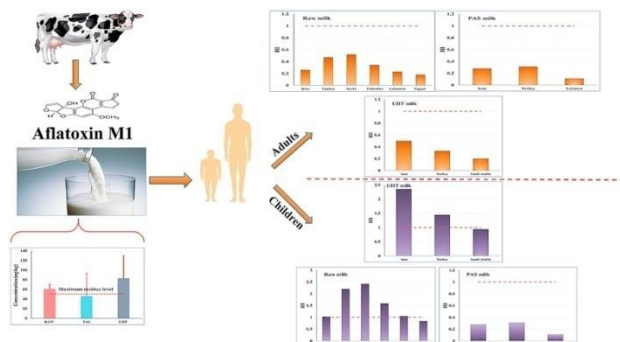
Through this kind of a study we could likely identify the antiviral activity of areca nut extract against Influenza virus and corona virus. Study may be conducted in-vitro methods. The symptoms and viral characters of Influenza and corona viruses are closely related to each other we could check the antiviral effect of the plant extract against both. In this way we hope to extract the antiviral agent against the present pandemic corona virus disease 19.

### *Areca catechu* nuts possess antifungal activity.



Aflatoxin in Sudan  
Survey and Determination of Aflatoxin Producing agents from Stored Peanut and Peanut Butter in Sudan

The investigations carried out indicates that the hot water extract of Areca catechu exhibits antifungal activity against unicellular yeast :*Candida albicans* , *Mucor sp*, *Aspergillus niger* , *Cladosporium sp* . Further studies are needed to determine the chemical identity of the bioactive compound responsible for the observed antifungal activity. The use of Arecanut extract in a dose dependant manner to prevent the aflatoxin production by *Aspergillus flavus* can be of industrial importance especially in chick feed industry , where aflatoxin has been a major poisoning agent due to the multiplication of the fungal contaminant *Aspergillus flavus*.



## Determination of Aflatoxins

- The determination of AFTs has been carried out using

- ✓ TLC
- ✓ HPTLC
- ✓ HPLC
- ✓ LC-MS
- ✓ immunological methods

Designed to detect the possible presence of AFTs B<sub>1</sub>, B<sub>2</sub>, G<sub>1</sub> and G<sub>2</sub> (Wolde, 2017).

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Betel nut chewing has been implicated as a cause of cancer. However chewing of tobacco along with betel nut may be the cause of oral cancer.. Arecanut chewing has been implicated as a cause of submucous fibrosis which is probably due to decreased collagen metabolism . Results of the investigation should be taken into perspective on the possible use of betel nut chewing in oral hygiene and possible inhibition of dental caries and oral candidiasis.

### Antioxidant activity of plant extract aqueous .Arecanut extract

Several plants and herbs are known to possess antioxidant activity. Arecanut extract has been reported to reduce the intracellular **reactive oxygen species**, ROS and release of myeloperoxidase by

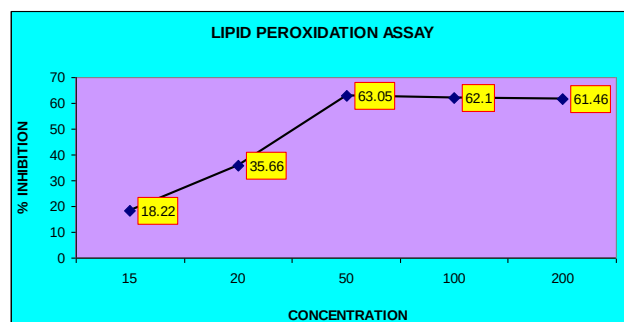
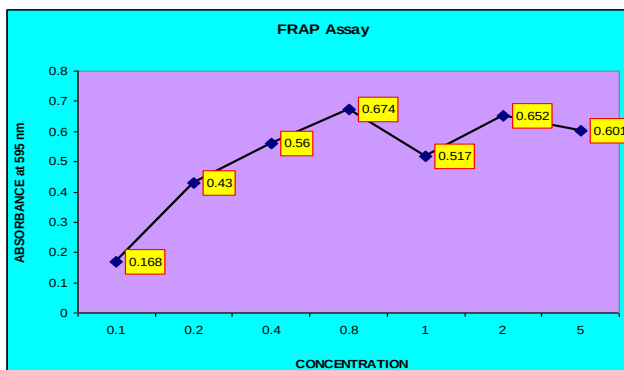
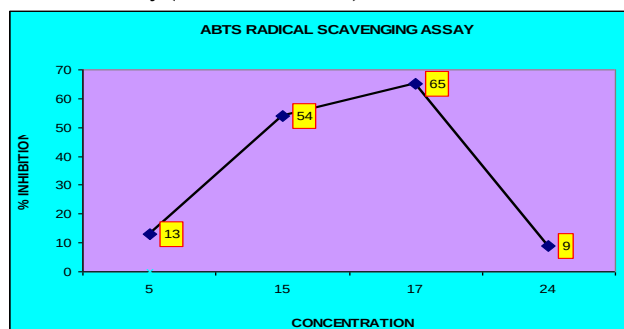
human polymorphonuclear leucocytes.. Organisms and humans possess several antioxidant systems –enzymatic and non enzymatic that are very important for the prevention of Oxidative stress.. Given the multiplicity of antioxidant pathways the centrality and prevalence of oxidant stress and the influences of lifestyle and nutritional supplements on an individual's antioxidant capacity, it is important to quantitatively assess the total antioxidant capacity or antioxidant power within biological specimens. Mitochondria are the major source for endogenous ROS production. Inducing oxidative stress by toxic chemicals may impair mitochondrial functions and bioenergetics leading to dysregulation of cell cycle control and apoptosis and necrosis. This is seen in cancer. Cellular GSH is the principal detoxifying system capable of scavenging ROS and maintaining the redox state of cellular thiols. Depletion of cellular thiols may lead to cellular oxidative stress. This is seen in cancer. The in vitro antioxidant studies on Arecanut like: Effect

of Arecanut extract on the inhibition of superoxide radical production

Effect of Arecanut extract on the inhibition of Hydroxyl Radicals

Effect of Arecanut extract on inhibition on of lipid peroxidation

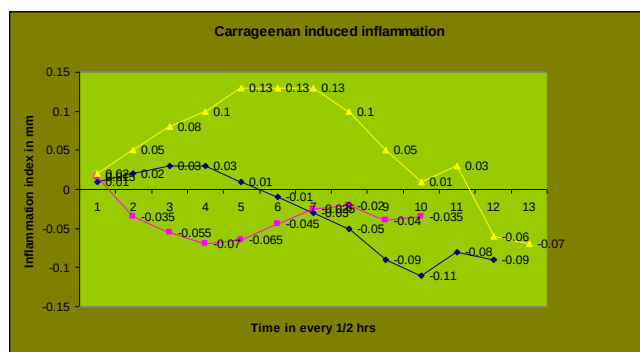
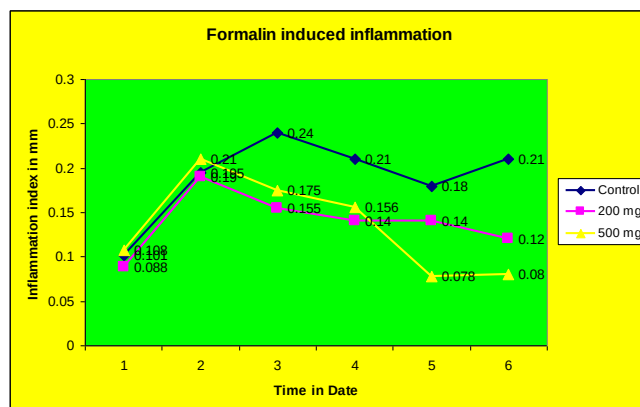
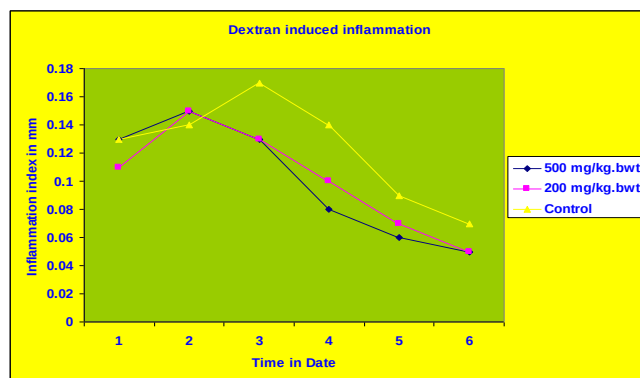
Effect of Arecanut extract on DPPH Radical scavenging activity(Diphenyl 2-Picryl Hydrazyl) Effect of Arecanut extract on ABTS Radical scavenging activity (Diammonium Salt)



Effect of Arecanut extract on Ferric Reducing Antioxidant Power(Tripyridyl-S-Triazine, Ferric chloride and Acetate buffer)

showed that arecanut extract does not produce any oxidative stress and has significant antioxidant potential and could scavenge free radicals effectively in vitro. Free radical scavenging activity of Arecanut extract , is a parameter for rating the value of an anticancer agent.

Anti-inflammatory activity of plant extract namely aqueous Arecanut extract:



Arecanut extract was effective in reducing the inflammatory oedema in animal studies using mice, where inflammation was induced by using carrageenan, dextran and formalin. Anti inflammatory activity of extract was in a dose dependant manner. Further investigations using various other animal models should be pursued followed by clinical trials to be recommended for use of arecanut extract for management of inflammation.



#### Anti-ulcerogenic activity of aqueous Arecanut extract:

Most anti-inflammatory drugs are ulcerogenic. NSAIDs (Non steroid anti inflammatory drugs) injure the gastrointestinal mucosa through oxygen derived free radicals and hence scavenging of noxious free radicals may produce beneficial effects in preventing the initiation of tissue injury and subsequent ulceration. Ethanol which induces ulcer was used as the ulcerogenic agent in the animal studies. Arecanut extract pre treatment has been shown to scavenge superoxide and hydroxyl radicals in vitro. Hydrolysable tannins in the purified arecanut extract induced a dose related increase in oxidative free radical scavenging enzymes such as superoxide dismutase, catalase and glutathione peroxidase and reduced lipid peroxidation in rat brain. The tannins may bind to membrane proteins and protect the gastric mucosa from the damage caused by ulcer. Hence it can be said based on animal studies that arecanut extract produced significant anti ulcer activity, which could be due to antioxidant activity and cytoprotection of gastric mucosa by tannins. Further investigations and clinical trials must be carried out to establish the antiulcerogenic effect of *Areca catechu*.

#### Aphrodisiac activity of Arecanut extract:



Arecanut has merited the role of improving male sexual activity. The significant and sustained increase in the sexual activity of male rats without any conspicuous adverse effects or toxicity suggest that Arecanut extract possesses clinically applicable activity and also lends support to the claims for its traditional usage as a sexual function enhancing medicine. Furthermore animal studies indicate that the aphrodisiac effects of the extract may be due to its psychoactive properties. It stands in good chance to be a safe alternative remedy for the treatment of sexual disorders.

Arecanut extract may be used as an adjunct in chemotherapy with Drugs that alter hormonal milieu eg: Estrogens used to treat prostate carcinoma.

#### Turmeric an anticancer agent



Turmeric or *Curcuma longa* has potential anticancer activity. Turmeric is a common spice used in daily curries in South India. Moreover turmeric has been prescribed for many ailments in Indian natural medicines. It is applied to fresh wounds and bruises and also act as a counter-irritant in insect bites. Internally it is an

anthelmintic. Turmeric paste is applied to facilitate the process of scabbing in chicken pox and small pox. It is also used in many urinary diseases, diseases of liver and in jaundice. Turmeric has been described as a cancer remedy in Indian natural medical literature. Turmeric extract and curcumin isolated from it, is highly cytotoxic to mammalian cell and is effective in reducing animal tumors, indicating its potential for use in cancer treatment.



### Marigold flower extract has potential antifungal activity:

Antifungal activity of *Calendula officinalis* (**regional name marigold**) flower extracts have been investigated against *Aspergillus niger*, *Rhizopus japonicum*, *Candida albicans*, *Candida tropicalis* and *Rhodotorula glutinis*. The inhibitory effects of extracts are very close and comparable in magnitude with that of standard antibiotics used.

### Antitumour activity of Picroliv

*Picrorhiza kurroa* (regional name: Kutki) forms an ingredient of many Indian herbal preparation used for the treatment of liver ailments. Picroliv is a standard preparation containing a purificate of the ethanolic extract of the roots and rhizomes of the *Picrorhiza kurroa*. Picroliv has been reported to be a potent hepatoprotective agent against various hepatoxins including hepatitis B virus. Picroliv has been shown to scavenge superoxide anions and induce glutathione-S-transferase. In addition it could reduce the increased level of lipid peroxidation products induced by (parasite) *Plasmodium berghei* in liver and brain of African desert rat resulting in recovery of reduced glutathione levels and activities of glutathione related enzymes. Studies have been done in Amala Cancer Research Centre, Thrissur, Kerala on the antioxidant activity of Picroliv. Studies have also been done to assess the effect of Picroliv treatment on ascites and solid tumor development induced by transplantable tumors in mice. The results showed the protective activity of Picroliv mixture isolated from *Picrorhiza kurroa* against chemically induced tumors. Picroliv treatment could significantly inhibit hepatocarcinogenesis induced by NDEA (N-NITROSO DIETHYL AMINE). This was reflected in the absence of tumors in Picroliv treated groups. (animal study using rats)

The chapter deals with the use of traditional plants used by Indian population for various ailments and maintenance of health. The history of use of these plants by human population and general human acceptance, common practise in ancient forms of medicine, high efficacy against multiple sites and capability of oral consumption warrants clinical trials in population with high cancer risk.

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