ejpmr, 2016,3(9), 395-400.

SJIF Impact Factor 3.628

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 3294-3211

EJPMR

A REGIONAL SURVEY ON THE BENEFITS OF OXIDATIVE STRESS MANAGEMENT AS CANCER THERAPY IN KERALA

John Thomas*, Jisha James and Arun M. S.

KVM College of Pharmacy, Kokkothamangalam P.O. Cherthala, Kerala India.

***Correspondence for Author: John Thomas**

KVM College of Pharmacy, Kokkothamangalam P.O. Cherthala, Kerala India.

Article Received on 03/07/2016 **Article Revised on 24/07/2016** **Article Accepted on 14/08/2016**

ABSTRACT

Socio-economic status of Kerala boost the practice of fast food culture in life. Importing of food items from other states leads to adulteration of food item and this intensified uses of pesticides. Research has revealed that the continued oxidative stress can lead to chronic inflammation, which in turn could mediate most chronic diseases including cancer, diabetes, cardiovascular, neurological and pulmonary diseases. Chemotherapy including immunotherapy, radiation are still prominent as the ways of treatment for cancer. In the survey we had analyzed, the benefits of a practicing method as cancer therapy in Kerala by using plant extracts of *Simarouba glauca* and *Annona muricata* to reduce the oxidative stress. The survey results found that it was effective against various type of diseases especially different types of Cancers to prevent it's progression. We have seen that the decoction taken as per guidelines given by 'Swanthana sparsam' organization, Trichur was highly effective and is able to manage cancer to a wide extend. Along with this, the comparison study of the cost effectiveness of the treatment has seen that the oxidative stress management is highly cost effective and showed better results and many of the people surveyed are leading normal life in comparison to the modern medicine.

KEYWORDS: Oxidative stress management, cancer, reactive oxygen species, guidelines.

INTRODUCTION

Oxidative stress is defined as an imbalance between production of free radicals and reactive metabolites, so-called oxidants or reactive oxygen species (ROS) and their elimination by protective mechanisms, referred to as antioxidants. This imbalance leads to damage of important biomolecules and cells, with potential impact on the whole organism.[1] ROS are products of a normal cellular metabolism and play vital roles in stimulation of signaling pathways in plant and animal cells in response to changes of intra- and extracellular environmental conditions.[2] Most ROS are generated in cells by the mitochondrial respiratory chain.[3] During endogenous metabolic reactions, aerobic cells produce ROS such as superoxide anion (O_2^-), hydrogen peroxide (H_2O_2), hydroxyl radical (OH•) and organic peroxides as normal products of the biological reduction of molecular oxygen.[4] The electron transfer to molecular oxygen occurs at the level of the respiratory chain and the electron transport chains are located in membranes of the mitochondria.[5,6] Under hypoxic conditions, the mitochondrial respiratory chain also produces nitric oxide (NO), which can generate other reactive nitrogen species (RNS).[3]

Extensive research during last two decades has revealed the mechanism by which continued oxidative stress can lead to chronic inflammation, which in turn could mediate most chronic diseases including cancer, diabetes, cardiovascular, neurological and pulmonary diseases. Oxidative stress can activate a variety of transcription factors including NF-κB, AP-1, p53, HIF-1α, PPAR-γ, β-catenin/Wnt, and Nrf2. Activation of these transcription factors can lead to the expression of over 500 different genes, including those for growth factors, inflammatory cytokines, chemokines, cell cycle regulatory molecules and anti-inflammatory molecules.[5]

Annona muricata "Fig.1" belongs to the family of Annonaceae has a widespread pantropical distribution and has its native in Central America. Intensive chemical investigations of the leaves and seeds of this species have resulted in the isolation of a great number of acetogenins. The isolated compounds display some of the interesting biological or pharmacological activities such as antitumoral, antiparasitic, cytotoxic and pesticidal properties. Roots of these species are used in the traditional medicine due to their ant parasitical and pesticidal properties.[7]

The seeds and leaves of these species was found to contain more than 50 mono-THF acetogenins. These acetognins has been isolated from this species recently and were named as epomuricenins-A and B,

montecristin, cohibins-A and B, muridienins-1 and 2, muridienins-3 and 4, muricadienin and chatenaytrienins-1,2 and 3 and also a new compound called as Sabadelin which might be a biogenetic precursor of cis-pantellin. Annonaceous acetogenins from its bark, seeds, and leaves which posses much of the diverse biological activites. The leaves of *A.muricata* has been resulted in the isolation of 8 cytotoxic acetogenins.[8]

Annonaceous acetogenins are a series of polyethers which contains either the adjacent or the nonadjacent tetrahydrofuran[THF] or tetrahydropyran[THP] ring and also an a,b-unsaturated c-lactone ring. They possess the most beneficial antitumor, cytotoxic, antimalarial and antifeedant properties. Acetognins gets interacted with the NADH-ubiquinone oxidoreductase in mamalian and in the insect mitochondrial electron transport system and or with biquinone-linked NADPH oxidase in the cancer cells cytoplasmic membrances.[9]

Simarouba glauca "Fig. 2" is commonly known as Laxmitaru or Paradise tree belonging to family Simaroubaceae. The leaves and bark of Simarouba have long been used as a natural medicine in tropics. French explorers noticed that the indigenous India tribes in the Guyana rainforest used *Sima rouba* bark as an effective treatment for malaria and dysentery. Other indigenous tribe throughout the south uses bark for fevers, malaria and dysentery as a haemostatic agent to stop bleeding and as a tonic. In cuba, where it is called gavilan, an infusion of the leaves or bark is considered to be astringent and used as a digestion and menstrual stimulant and an antiparasitic remedy. It is taken internally for diarrhea, dysentery, malaria and colitis. It is used externally for wounds and sores. Bark and leaf of Simarouba contain triterpens useful in curing amoebiasis, diarrhea and malaria. The chemicals present in leaf, fruit, pulp and seed of *S.glauca* are known to posses the medicinal properties such as analgesic, anti microbial, anti viral, astringent, stomachic and tonic.[10]

An infusion of the bark is used against malaria, rheumatism, shingles and fever. It also posses antiprotozal and antibacterial activities. They are useful in curing amoebiasis, gastritis, ulcers in alimentary systems, chikun gunya and malaria. The quassinoids, glaucarubin along with glaucarubinone and glaucarubol from the seeds of *S.glauca* showed promising activity against *Plasmodial falciparum* in culture. *S. glauca* have exhibited cytotoxic activity invito against human oral epidermoidal carcinoma. [11]

Ascorbic acid (AA), commonly known as vitamin C plays an important role in the human body and is necessary for the synthesis of collagen, a protein that has many connective functions in the body. Its antioxidant capacity is associated with reduced incidence of cancer.[12] Some epidemiological data mentioned its usefulness in reducing cold with increasing consumption of foods rich in vitamin, so people sometimes ingest an overdose of it. In most reports mention that discrete increases in blood levels of this vitamin reduces the risk of death in all conditions.[13] The combination of vitamin C and vitamin K already given in the chemotherapy increases the survival and the effects of various chemotherapeutic agents in a tumor-ascitic- murine model. The co administration of vitamin A, β-carotene, E and C can reduce the incidence and delay the progression of several cancers, such as skin, colon, stomach, esophagus, mammary gland and matrix. There are a decrease in the risk and incidence of cancer in populations with high content of vitamins in plasma.[14]

Socio-economic status of Kerala is comparatively above the average of other states of India. It depends on the earning of family members. The percapita income boost up to lead modern life. So people adopt the practice of fast food and life style has changed. In the long run of this busy life people deviated away from the ayurveda, “the practice of life”. So people scarifies many of the ayurvedic living practices. This boost up the life style diseases among Kerala people. It finally increases the oxidative stress which may lead to cancer.[5]

MATERIALS AND METHODS

In the present study we had analyzed, the effect of the decoction of *Simarouba glauca* and *Annona muricata* against various type of cancers by written and oral interview of 67 cancer patients at different stages of disease progression. The disease stage is identified from the pathology reports. We also analyzed the effect of these two plants on the oxidative stress management for cancer therapy as per 'guidelines' given by Dr. Augustine Antony under the organization, Swathana Sparsam, Thrissur under the programme-PULSE in the prevention and further progress of various Cancers by oxidative stress management. Along with this we also focused on the correlation of the expenses for the treatment by modern medicine and the oxidative stress management therapy. For the better results by oxidative stress management therapy, Dr. Augustine also introduced some 'guidelines' to follow for the better results. The guidelines are:

- ✓ Drink sufficient of fresh water and avoid artificial drinks like soda, cola etc. Coconut water is suitable to drink.
- ✓ Avoid food items containing artificial flavor additives, stabilizers and preservatives.
- ✓ Avoid tea, coffee, salt, sugar etc if necessary green tea [organic] can be used. Avoid the habit of consumption of alcohol and tobacco.
- ✓ Avoid the use of fried food items.
- ✓ Avoid meat, egg, milk, fish, etc. Use cashew nut, pulses, fruits in diet.
- ✓ Use plenty of pesticide free vegetables mainly leafy vegetables in diet
- ✓ Always do breathing exercise, yoga, etc. Patients should accommodate only in well ventilated rooms with good air circulation.

Based on this, we have conducted a detailed survey of various cancer patients who followed and not followed the 'guidelines' along with the patients who were continued the normal chemotherapy and radiation methods. We also interviewed 20 people who used to take this medication as a preventive in every 6 months.

Method of Preparation of extracts

Simarouba glauca extract has to be prepared on the principle of fractional distillation method. A quantity of 3 leaves per 10 kg of the patient's weight has to be taken and extracted by hot extraction method in approximately about 600 ml of water and reduced to 200 ml by boiling and served before food. The leaves are further extracted with the same quantity of water and make ready for noon meal and served half an hour before the meal. Repeat this process and make ready 200 ml for dinner and serve half an hour before the dinner.

After half an hour, the patient is allowed to take routine food along with vitamin C. After half an hour of food, the prepared *Annona muricata* leaf extract prepared as per the quantity of 3 leaves per 10 kg of the patient and extracted by hot extraction by boiling leaves in approximately 1000ml of water and reduced to 600 ml so as to divide it into 200 ml each and served for three times after half an hour of the food. All these extracts should be prepared in clay pots or stainless steel vessels. The remaining diet should follow as per the guidelines.

RESULTS AND DISCUSSIONS

Reactive oxidative species are products of a normal cellular metabolism and play vital roles in stimulation of signaling pathways in plant and animal cells in response to changes of intra- and extracellular environmental conditions.[5] In an effort to reduce the oxidative stress and get a cure for many ailments including cancer, Dr. Augustine Antony, a biotechnologist, in association with the organization, Swanthana sparsam -PULSE, implemented the guide lines to reduce the oxidative stress through the usage of anti oxidant rich food along with decoction of the plant leaves of *Simarouba glauca* and *Annona muricata*.

Comparative analysis of patients followed Chemotherapy & Guidelines

In the new social background of Kerala, the number of cancer cases are increasing day by day and most of them prefer chemotherapy than any other modes of treatments. In our study of 67 cancer patients, 44 underwent modern medicines for the survival than other modes of treatment. 23 patients underwent the oxidative stress management therapy due to knowledge of effectiveness of this method from their friends or awareness lectures delivered from Swanthanasparsam organization during the awareness campaign as depicted in "Fig 3". Many are doubtful about the effectiveness and the outcome of results on this therapy. Some others are not relied due to the presence of other life style diseases like diabetic, blood pressure etc. Out of 67 patients surveyed, cases of breast cancer and prostate cancer was reporting more in number than others "Fig 3".

Age group of surveyed patients

Many reports are available about the age group of cancer patients. In our study the age group of patients involved in the survey has observed that the age group starts from 30- 78years and average age group is 50-60 years "Fig 4". Breast cancer and uterus cancer normally found in the age group of 50 years where as prostate, lung and colon cancer majorly found at an age group of 60 years.

Limit of Cure-current status

All the cancer patients who underwent modern medicines and oxidative stress therapy as per 'guidelines' are getting the cure to a limit depends on the age group and other diseases associated with the patient. We are surprisingly noted that all the type of cancer patients who followed the guidelines are surviving with a healthy life and most of them were back to their normal life. They are leading a normal life with utmost care to follow the 'guidelines'. Some of the patients deviating from the food habit i.e. consuming animal protein in the form of meat, fish, chicken, egg, milk etc are getting some kind of weakness. we observed this opinion on discussion with the patients as in table 1.

In those patients depending on the modern medicine including chemotherapy, radiation and surgery have much side effects and many of them are living in the feeling of a dreadful disease. Some patients underwent surgery are completely bedridden. The worst of this condition has observed with patients underwent radiation therapy. They are living with deformalities and many are unable to recover the normal life. So oxidative stress therapy was found to be much effective to lead a normal life during the treatment. The extent of cure depend on the stages and other associated ailments of patients.

The fast food culture due to commercialization may be one of the major reason for irrational spreading of cancer cases. People start purchasing eatables including staple food like rice, vegetables etc from the neighboring states with a cheaper rate than producing these items with in the state. So people gradually move away from cultivation. The government policies also boost the situation. This intensified the adulteration of food items and use of pesticides in various varieties. Due to lack of any more economically cheaper and better choices, people force to consume it and became their life style. This may helps to spread the disease of cancer embarrassingly. It affect all the age group from the birth onwards. Many are remaining as carriers of Cancer.

The cost of treatment, starting from diagnosis to medications affected the economy of people. The mode of treatment from the diagnosis made the patient as real sick and the deformalities happen during the radiation therapy made a social stigma and side lined those people from society. By the end of 2010, many agencies start

reporting the fact and government slowly start making awareness among people. They start promotions of cultivation of vegetables indigenously.

Cancer treatment is highly expensive and cannot afford by many people. Based on the cultural set up of Kerala, all have an intense relationship with in the family. So most of them are trying to give best treatment to their dear ones. Some are affordable and for many of them it is not affordable. So they used to lend or sell their properties for getting enough money for treatment and ultimately leads to bankruptcy and poverty.

In the oxidative stress management treatment the expenses are dramatically reduced because the leaves are collecting by the patient or relatives which will not cause much expense. A maximum of INR 3000 used to meet by the patient and getting a maximum cure by oxidative stress management therapy. But the treatments by modern medicines causes a high loss of economy for the patient's family and an average monthly expense touches above INR 10000 as in Table 2.

As a preventive medicine

The oxidative stress management is not only used for the management of cancer but also for the many other ailments such as varicose vein, diabetics, anti-inflammatory etc as per our survey report.

Table1. Comparative study of patients using *Simarouba glauca* and *Annona muricata* as cancer therapy medicine.

Type of Cancer	Patients who followed the guide lines and treat with *Annona muricata* and *Simarouba glauca*						Modern medicine including chemotherapy &radiation					
	Number of patient in each stages of Cancer					Limit of Cure or current status	Number of patient in each stages of Cancer					Limit of Cure or current status
	TotalNos	1	2	3	4		TotalNos	1	2	3	4	
Breast Cancer	6	4	2			No further progression, leading normal life	20	9	8		3	12 patients under gone surgery and many have side effects of chemotherapy
Pancreas Cancer	2		2			No further progression, leading normal life	4		4			Out of 4 , 2 are surviving with no further progression, but has much side effects of chemotherapy
Lung Cancer	3	2	1			Breathing trouble, but no further progression	5	1	4			Severe asthmatic problem & much side effects of chemotherapy & radiation
Prostate Cancer	4		3		1	Leading normal life	6	4	2			Undergone surgery and radiation
Uterus Cancer	4	3	1			Some undergone surgery , leading normal life	4	3	1			Most of them undergo chemotherapy &3 leading normal life
Lymphoma Cancer	1		1			Leading normal life	1		1			Side effects of chemotherapy
Appendice Cancer	1	1				Leading normal life	2	1	1			Side effects of chemotherapy
Blood Cancer	1		1			Leading normal life	1		1			Side effects of chemotherapy
Colon Cancer	1			1		Leading normal life	1		1			Side effects of chemotherapy

NOTE: *Some of the patients started using Simarouba glauca and Annona muricata, but discontinue and restarted Chemotherapy.*

Table 2 Comparative analysis of expenditure in oxidative stress management and modern medicine.

Type of Cancer	Patients who followed the guide lines and treat with *Simarouba glauca* and *Annona muricata*		Modern medicine including chemotherapy &radiation	
	No. of patients	Expenditure per month in Indian National Rupee (INR)	No. of patients	Expenditure per month in Indian National Rupee (INR)
Breast	6	500-1000	20	5000-10000
Pancreas	2	500- 2000	4	10000-15000
Lung	3	500-3000	5	15000-20000
Prostate	4	500-2000	6	5000-6000
Uterus	4	500-1000	4	500-1000
Lymphoma	1	500-1000	1	5000-10000
Appendices	1	1000-3000	2	5000-10000
Blood	1	1000-3000	1	5000-10000
Colon	1	1000-3000	1	5000-10000

Fig 1 ***Annona muricata***

Fig 2 ***Simarouba glauca***

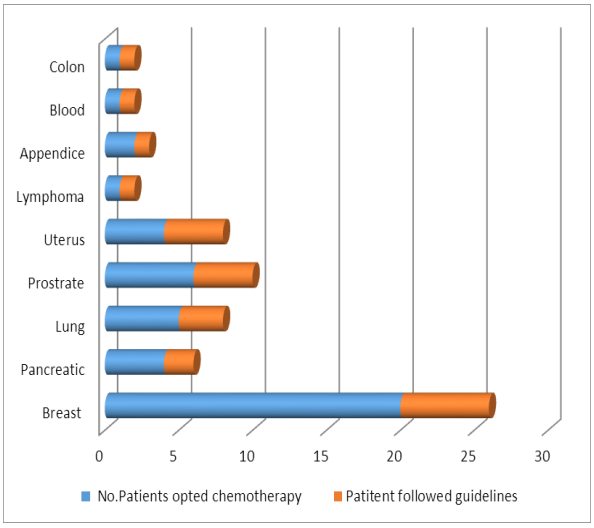

Fig 3. Number of surveyed cancer patients who preferred chemotherapy and guidelines of oxidative stress management

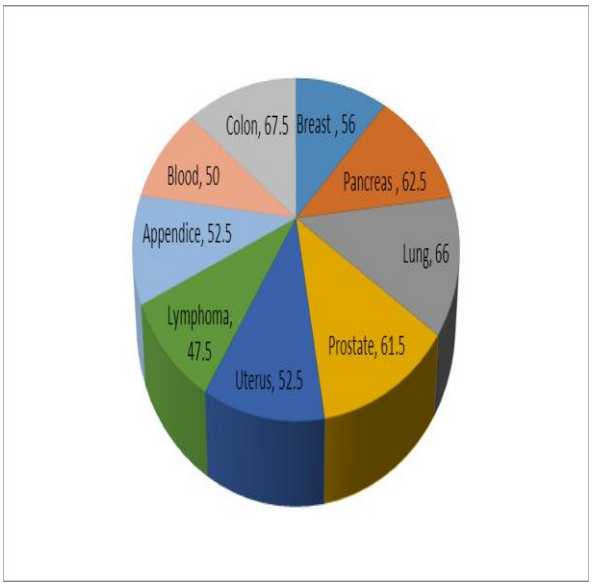

Fig 4 Average age group of surveyed cancer patients

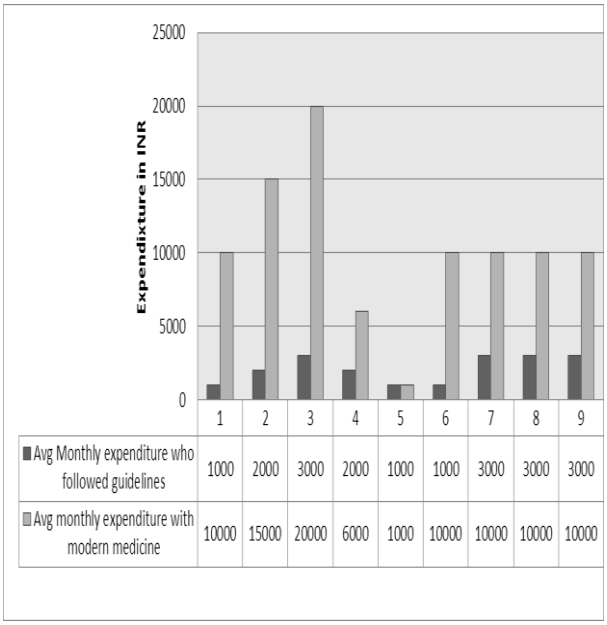

Fig 5. Comparative analysis of average monthly expenses for treatment in Indian National Rupee (INR).

CONCLUSION

A survey has done to find the efficiency of oxidative stress management over the modern medicines for cancer therapy. Survey reports showed that the oxidative stress management therapy by following guidelines of Swanthanasparsam organization was highly effective in cancer management and many are leading normal life. It was also found to be effective for the management of many life style diseases.

ACKNOWLEDGEMENT

We acknowledge Dr. Augustine Antony and Jigi T. John, Pollackattu for the valuable information in the completion of survey.

REFERENCES

1. Durackova Z. Some current insights into oxidative stress. Physiol Res. 2009.
2. Jabs T. Reactive oxygen intermediates as mediators of programmed cell death in plants and animals. Biochem Pharmacol. 1999; 57: 231–245.
3. Poyton RO, Ball KA, Castello PR. Mitochondrial generation of free radicals and hypoxic signaling. Trends Endocrinol Metab. 2009; 20: 332–340.
4. Fridovich I. The biology of oxygen radicals. Science. 1978; 201: 875–880.
5. Goossens V, De Vos K, Vercammen D, Steemans M, Vancompernolle K, Fiers W, Vandenabeele P, Grooten J. Redox regulation of TNF signaling. Biofactors. 1999; 10: 145–156.
6. Goossens V, Grooten J, De Vos K, Fiers W. Direct evidence for tumor necrosis factor-induced mitochondrial reactive oxygen intermediates and their involvement in cytotoxicity. Proc Natl Acad Sci U S A. 1995; 92: 8115–8119.
7. Christophe G, Alain L, Reynald H, Olivier L, Laurent S and Andre C. Cohibins A and B, Acetogenins from roots of *Annonamuricata*. Phytochemistry, 1997; 44(8): 1541-1545.
8. Geum-soog K, Lu zeng, Feras A, Lingling L R, Fengewu, Soelaksono S, Jerry L. Mclaughlin. Muricoreacin and murihexocin C mono-tetrahydrofuran acetogenins from the leaves of *Annonamuricata.* Phytochemistry. 1998; 38(1): 454-460.
9. Pathak P, Saraswathy Dr, Vora A, Savai J. In vitro antimicrobial activity and phytochemical analysis of the leaves of *Annona muricata*. International Journal of Pharma Research and Development. 2010; 2(5).
10. Bhagmal. Sustainability in oil seeds, Indian society of oil seed Research, Hyderabad. 1994; 83-90.
11. Iasmine ABS. Alves, Henrique MM, Luiz A.L. Soares, Karina P. R. Simaroubaceae family: botany, chemical composition and biological activities. Rev Bras Farmacogn. 2014; 24: 481-501.
12. Akhilender NK. Vitamin C in human health and disease is still a mystery? An overview. Nutr J. 2003; 2: 1475-2891-2-7.
13. Anitra C Carr and Balz Frei. Toward a new recommended dietary allowance for vitamin C based on antioxidant and health effects in humans Am J Clin Nutr. 1999; 69: 1086–107.
14. Chen Qi, Espey M G, Krishna MC, Mitchell JB, Corpe CP, Buettner GR, Shacter E, Levine M. Pharmacologic ascorbic acid concentrations selectively kill cancer cells: Action as a pro-drug to deliver hydrogen peroxide to tissues. PNAS, 2005; 102(38): 13604-13609.