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Research Article

"ASSESSMENT OF ANTI-OXIDANT ACTIVITY OF *YASTIMADHU (GLYCYRRHIZA GLABRA LINN.)* WITH SPECIAL REFERENCE TO SMOKING INDUCED OXIDATIVE STRESS."

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ABSTRACT

Smoking is a serious health problem causing *pranavahastrotodushti*. Cigarette smoke emits free radicals, excess of which leads to increased oxidative stress. There are not many medicines available to prevent or decrease this oxidative stress. *Yashtimadhu* (*Glycyrrhizaglabra Linn*.) has a sufficient proof as an anti-oxidant and plays a very important role on *pranavahastrotodushti*. Open labelled controlled study was done on 60 smokers who had smoked more than 5 cigarettes per day continually for at least 3 years at AyurvedMahavidyalayaSion, Mumbai-22 for duration of 60 days. Out of 60 smokers, 30 were advised to take *Yastimadhughanavati* 1 gm twice a day with warm water while 30 were controlled group.Subjective assessment was done with the help of signs & symptoms like *kasa, sakashtaucchawas, pinasa, ghurghuryuktashwas, swedapravrutti, kastenshleshmavimokshana* every fortnightly. Objective improvement was done on the basis of PEFR (Peak expiratory flow rate test)**,** and MDA (Malondialdehyde), GSH (glutathione peroxidase) and SOD (Superoxide dismutase) enzyme study for anti-oxidant activity at baseline and at the end of study. Subjective improvement is shown in percentage. There was significant improvement in symptoms in Group A as compared to Group B. Unpaired t test was applied to objective parameters which was highly significant at 5% level of significance i.e. $p<0.01$ for PEFR test and at 1% level of significance i.e. $p<0.01$ for anti-oxidant enzymes concluding *Yastimadhu*(*Glycyrrhizaglabra Linn*.) definitely has anti-oxidant activity.

Keywods: Smoking, Oxidative stress, *Yastimadhu (Glycyrrhizaglabra Linn.)*, anti-oxidant, MDA(Malondialdehyde), GSH (Glutathioneperoxidase), SOD (Superoxide dismutase).

INTRODUCTION

Cigarette smoking is a serious health problem and most important avoidable causes of death in world. There are approximately 120 million smokers in India. According to the World Health Organization (WHO), India is home to 12% of the world's smokers. Smoking kills 900,000 people every year in India. Smoking may soon account for 20 % of all male deaths and 5 % of all female deaths among Indians between the ages of 30 and 69. [1]Smoking being a major risk factor for many diseases like myocardial infarction, Chronic Obstructive Pulmonary Disease (COPD)

emphysema, and cancers, particularly lung cancer, cancers of the larynx and mouth, and pancreatic cancer.[2]Overall life expectancy is also reduced in long term smokers, with estimates ranging from 10 to 17.9 years fewer than non-smokers. [3] Cigarette smoke is a complex mixture of chemicals containing more than 4000 different constituents.Nicotine, carbon monoxide, and tars are some of these substances[4]Smoking has been implicated as a major cause of increased oxidative stress.Oxidative stress is an increased exposure to oxidants and/or decreased antioxidant activityand is widely recognized as a central feature of many diseases. Free radical-induced oxidative damage has been suggested to play a major role in the pathogenesis of numerous smoking-related disorders.[5]Tobacco smoke is a rich source of oxidants. The inhalation of cigarette smoke triggers a marked cellular influx in the lung, and this inflammation is believed to play a central role in the development of smoke related lung diseases.[6]Ayurvedic drugs like *Shatavari(Asparagus racemosaWilld), Guduchi (TinosporacordifoliaWilld), Gokshur (Tribulusterrestris Linn.), Ashwagandha (WithaniasomniferaDunal), Pippali (Piper longum Linn.), Amalaki (EmblicaofficinalisGaertn.), Dadima (Punicagranatum Linn.), Tulsi (Ocimum sanctum Linn.), Haritaki (Terminaliachebula Retz.), Bibhitaki (TerminaliabellericaRoxb.), Ardrak (Zingiberofficinale Linn.)* etc. possess anti-oxidant properties.[7]*Yastimadhu (Glycyrrhizaglabra Linn.)* is one such drug. *Yastimadhu* has *Madhura rasa, madhuravipaka&sheetavirya*.[8]. It is a rich source of flavanoids and polyphenols which show anti-oxidant properties.[9] Flavonoids from licorice are currently the strongest natural antioxidants known. Its major Chemical constituents are glycyrrhizin, flavones, coumarins and polyphenols. Cigarette smoking vitiates ruksha, tikshna and usnaguna in the body.Smoking greatly affects lungs and airways. Smokers get affected with variety of problems related to breathing. Problems range from an annoying cough to grave illness like emphysema and cancer.[10]PEFR(Peak expiratory flow rate) is a simple index of pulmonary function and reflects the status of large airways. It measures person's maximum speed of expiration, as measured with a peak flow meter. It measures the airflow through the bronchi and thus the degree of obstruction in the airways. Peak flow readings are higher when patients are well and lower when the airways are constricted.[11]MDA is an oxidative stress marker and hence decreases in MDA results in decreased oxidative stress. SOD and GSH are enzymatic and non-enzymatic defence systemwhich increases on decrease in oxidative stress.[12]

MATERIALS AND METHODS

Selection of cases: There was random selection of patient from O.P.D. and I.P.D. of ShethR.V. Ayurvedic hospital, Sion, Mumbai-22. Study was carried out as per Ethical Clearance Number –AMS/ 1787/ 12-13

Type of study: Open labeled controlled study

Study Design: 60 patients

Group A : 30 patients were given*YastimadhuGhanavati.*

Group B : 30 patients were of controlled group.

Duration of study-60 Days

Inclusive criteria

- Subjects smoking 5 or more cigarettes per day and smoking period not less than 3 years.
- Sex : both Male & Female
- Age between 20-60 years
- Informed consent signed

Exclusive criteria

- Age less than 20 years and more than 60 years.
- Subjects smoking less than 5 cigarettes per day or smoking period less than 3 years.
- Dyspnea due to other causes like obesity, anemia, ascites, CCF, etc.

- Dyspnea due to local cause like lung abscess, pneumonia, lung congestion, tumors of respiratory tract.
- On drugs:- Anti-convulsants, Anti-psychotic/ Anti-depressants, Steroids Dependents.
- HIV or HbsAg +ve smokers.
- Smokers with other systemic illness like CA, Koch's, cirrhosis of liver or any other any major illness.

Drug source: Coarse powder of Root of *Yastimadhu(Glycyrrhizaglabra Linn.)*

Formulation: *Ghanavati* of *Yashtimadhu(Glycyrrhizaglabra Linn.)*

Mode of administration: Oral.

Dose: 1 gm BD

Anupan*: Koshnodak*(Warm water)

Follow up: Clinical follow-up was advised every 15 days in duration of 60 days.

Statistical test: Statistical analysis was done by applying Unpaired t-test to objective parameters: at baseline and at the end of study (after 60 days). Subjective improvement has been shown in percentage.[13]

Assessment of efficacy

Subjective improvement

Monthly assessment was done with the help of reduction in following symptoms.

- *Kasa* (Cough)
- *Sakashtaucchvasa*(Difficulty in expiration)
- *Pinasa*(rhinorrhoea)
- *Ghurghuryuktashvasa* (Rhonchi)
- *Swedapravrutti*(Sweating)
- *Kashtenshleshmavimokshan*(Difficulty in expectoration)

Objective improvement

- Peak expiratory flow rate(PEFR) test
- For antioxidant Study: MDA (Malionaldehyde), SOD(superoxide dismutase), GSH(glutathione) enzyme study

Gradation of symptoms [14]

1.*Kasa*(Cough)
0-absent
1-1 to 5 bouts in every three hours
2-5 to 10 bouts in every three hours
3-excessive coughing

2.*Sakashtaucchvasa* (Difficulty in expiration)
0-Absent
1-mild pain during expiration
2-moderate pain during expiration
3-severe pain during expiration

3. *Pinasa* (rhinorrhoea)
0- No rhinorrhoea
1-Lasting upto one week and don't require any specific treatment
2-lasting for more than one week & subside after primary medication
3-Continuous Rhinitis

4.*Ghurghuryuktashvasa* (Rhonchi)
0- Chest cleared on forced expiration
1-Rhonchi heard on forced expiration but not heard on deep breathing.
2-scattered rhonchi on normal deep breathing
3-Numerable high pitched rhonchi auscultated on normal deep breathing.

5. *Swedapravrutti* (Sweating)
0- No Sweating
1- Mild Sweating
2-Moderate sweating
3- Profuse Sweating

6.*Kashtenshleshmavimokshan*(Difficulty in expectoration)
0- absent
1-Scanty expectoration after 1 to 5 bouts
2-Scanty expectoration after 5 to 10 bouts
3-Scanty expectoration after more than 10 bouts.

Preparation of *Yashtimadhu Ghana*:[15]

Take coarse powder of Root of *Yashtimadhu*in pot in required quantity. Add 16 times water to the powder. Then keep pot on Gas. Always keep gas on

slow flame (*Mandagni*). When 1/8th water remains, decoction is ready. Filter the decoction with clean cloth and again keep the filtered decoction on slow flame. Then boil it further up to semi-solid consistency. Dry this Ghana.Make pills of 500 mg weight from the prepared Ghana.

RESULTS

Table 1 Chart Showing % Improvement In Symptoms

% IMPROVEMENT IN SYMPTOMS				
	GROUP A		GROUP B	
SYMPTOMS	%	SUBJECTS	%	SUBJECTS
Kasa	92.59	25 out of 27	14.28	4 out of 28
Sakashtaucchvasa	84.00	21 out of 25	5.00	1 out of 20
Pinasa	33.33	6 out of 18	41.66	5 out of 12
Ghurghuryuktashvasa	43.47	10 out of 23	10.00	2 out of 20
Swedapravrutti	46.66	7 out of 15	6.66	1 out of 15
Kashtenshleshmavimokshan	85.18	23 out of 27	18.75	3 out of 16

Table 2: PEFR Analysis

	Decreased	No change	Increased
Group A	**10 %**	**6.66 %**	**83.33 %**
Group B	**76.66 %**	**20.00%**	**3.33 %**

Table 3:Statistical analysis of PEFR

	Mean	SD	SE
Group A	**-17.66**	**13.56**	**2.47**
Group B	**9**	**7.58**	**1.38**

Table 4: MDA Analysis

	Increased	No change	Decreased
Group A	**96.67 %**	**3.45 %**	**0.00 %**
Group B	**10.00 %**	**0.00 %**	**90.00 %**

Table 3: Statistical analysis of MDA

	Mean	SD	SE
Group A	**1.85**	**1.16**	**0.21**
Group B	**-0.97**	**0.71**	**0.13**

Table 2: SOD Analysis

	Decreased	No change	Increased
Group A	**93.33 %**	**0.00 %**	**6.66 %**
Group B	**90.00 %**	**0.00 %**	**10.00 %**

Table 3: Statistical analysis of SOD

	Mean	SD	SE
Group A	**-0.71**	**0.44**	**0.08**
Group B	**0.38**	**0.29**	**0.05**

Table 2: GSH Analysis

	Decreased	No change	Increased
Group A	**3.33 %**	**0.00 %**	**96.67 %**
Group B	**93.33 %**	**0.00 %**	**6.66 %**

Table 3: Statistical analysis of GSH

	Mean	SD	SE
Group A	**-13.22**	**7.28**	**1.32**
Group B	**8.46**	**4.52**	**0.82**

Out of 60 patients 7 [11.67%] were females and 53[88.33%] were males.Agewise categorisation showed that 16.67% were between 20-30 years of age, 23.33% between 31-40 years of age, 31.67% between 41-50 years of age and 28.33% between 51-60 years of age.According to physical activity 11.67 % were heavy worker, 46.67% moderate worker and 41.67% were sedentary worker. Diet wise distribution shows that 38.33% 0f subjects have a vegetarian diet and 61.67% have mixed diet.Comparison of subjective evaluation between two groups showed that there was significant improvement in symptoms of group A as compared to group B. 92.59% subjects showed improvement in *kasa*, 84.00% subjects showed improvement in *sakashtaucchvasa*and 85.15% subjects showed improvement in *Kashtenshleshmavimokshan* as compared to group B, only 14.28%, 5%, and 18.75 % subjects respectively showed improvement. This difference may be due to *Yashtimadhu*. Unpaired t test was applied to objective parameters. It was observed that for PEFR, t value (9.397) was extremely significant at $p < 0.01$ concluding better results in Group A. Also after applying Unpaired t test for anti-oxidant enzymes the t value were 11.357, 11.206 and 13.862 respectively for MDA, SOD & GSH which are highly significant at $p < 0.01$.

DISCUSSION

Cigarette smoking mainly causes vitiation of, *vata, pitta* & *raktadosha* in the body. It predominantly affects *pranavahastrotas*. It causes increase in *laghu, ruksha* and chala*gunas* of *vata, tikshna, ushnagunas* of *pitta*and decrease in *snigdhagunas* of *kaphadosha*. The lungs produce mucus to trap chemical and toxic substances. Cilia coat the lungs airways and move rhythmically to clear this mucus from the lungs. Combined with coughing, this is usually an effective method of clearing the lungs of harmful substances. Tobacco smoke paralyzes these hairs, allowing mucus to collect in the lungs of the smoker. Cigarette smoke also promotes goblet cell growth resulting in an increase in mucus. More mucus is made with each breath of irritating tobacco and the smoker cannot easily clear the increased mucus. Smokers also suffer from painful heartburn and result in an increased risk of long term inflammation and dysfunction of the oesophagus and stomach. Smoking also increases reflux of stomach contents into the oesophagus and pharynx which increases acid exposure.

Yashtimadhu plays a major role on *pranavahastotas*(respiratory system). It is useful in *kasa*(cough), *shwaas* (asthma) and *svarabheda* (hoarseness of voice). It helps in easy expectoration of mucus. Because of its *snigdhaguna* it reduces the *rukshaguna* of *vata* and and improves the functioning of cilia and thus helps in effective clearing of lungs in smokers. It also acts as mild purgative and helps to relieve constipation. Because of its *sandhaniya* property it helps in healing of *urakshata, amashayikvrana* (Peptic ulcer) etc. Because of its *madhura rasa* it reduces heartburn and hyperacidity. Because of its *snigdhaguna* and *madhurarasa* and *vipaka* it acts as *kaphanissaraka* and *kanthya*. *Yashtimadhu* reduces oxidative stress by scavenging free radicals and terminating chain reaction. There was a considerable decrease in MDA values and good increase in GSH and SOD values in subjects taking *Yashtimadhu* as is evident from statistical analysis.

There were no major adverse events noted with *Yashtimadhu*. There were some minor problems encounterd by the subjects taking *Yashtimadhu*. It was noted that a few subjects experienced nauseating sensation while ingesting *Yashtimadhu* for first 3-4 days. Some could not tolerate its smell. But all these symptoms abated after 3-4 days. Also smokers have the habit of smoking during passage of stool in the morning. *Yashtimadhu*has the property of mild purgation. The complaint of constipation was relieved after taking *Yashtimadhu*.Further research needs to be done to make *Yashtimadhu* palatable.

CONCLUSION

After studying 60 patients for 60 days following points were concluded.

1) Patients taking *Yastimadhughanavati*have shown considerable decrease in subjective (signs and symptoms) and objective parameters (PEFR, MDA , SOD & GSH) as compared to other group. *Yastimadhu* having *madhurarasa*, *madhuravipaka, Sheetavirya and guru, snigdhaguna*which compensates the ruksha, tikshna and ushnaguna vitiated by cigarette smoking. It helps in easy expectoration of mucus which improves the functioning of cilia. It also reduces heartburn and hyperacidity. Thus it can be concluded that *Yastimadhu is* definitely helpful in smokers.

2) *Yastimadhu* reduces oxidative stress by scavenging free radicals and terminating chain reaction. There was considerable decrease in MDA values and good increase in SOD &GSH values in patients taking *Yastimadhughanavati*. Polyphenols and flavonoids present in *Yastimadhu* may be responsible for this.

3) The drug does not showed any toxic effects.

Thus *Yastimadhu* definitely has anti-oxidant activityin smoking induced oxidative stress and is effective medicine for smokers to make their prognosis better.

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