

# SYZYGIUM AROMATICUM: A POTENTIAL HEPATOPROTECTIVE AGENT

Sadia Kazi,<sup>1</sup> Palwasha Abbasi,<sup>1</sup> Ashique Ali Arain<sup>1</sup>

## ABSTRACT

**Background:** Syzygium aromaticum is commonly known as clove. It is being used since centuries for different purposes in different parts of the world. **Objective:** To explore the effects of Syzygium Aromaticum, its effects on the liver enzymes. **Methodology:** This Randomized Control Trial was conducted in Postgraduate Laboratory and Animal House of ISRA University. 30 Healthy Rabbits weighing 2kg on average were divided into 3 equal groups. Group A was taken as control group having no intervention while group B was given paracetamol 500mg BD for 10 days followed by Syzygium Aromaticum powder 100mg BD for next 10 days. Group C was given paracetamol 500mg BD and Syzygium Aromaticum powder 100mg BD for 20 days. Blood samples were taken from ear lobes through 24 gauge canula for liver enzymes at days 1, 10 and 20 and analyzed in ISRA Laboratory. Mean and standard deviation were calculated and p-value <0.05 was taken as significant. The data was entered and analyzed by using SPSS version 16. **Results:** There was no rise in liver enzymes in group A at any stage of the study. Liver enzymes ALT, AST, GGT, ALP and LDH markedly increased in group B in initial 10 days but declined in next 10 days. There was no significant rise in liver enzymes in group C at any level of the study. **Conclusion:** Syzygium aromaticum is an effective natural hepatoprotective agent.

**Key words:** Hepatoprotective, Alanine Transaminase, Alkaline Phosphatase, Aspartate Transaminase, Lactate Dehydrogenase, Gamma Glutamyl Ttransferase.

JSZMC 2016;7(2):956-959

## INTRODUCTION

Liver regulates the most of essential functions in the body. Exposure to potentially toxic compounds, contaminated foods, chemical substances of environment produces many side effects to human beings.<sup>1</sup> Liver function tests (LFTs) are the most commonly and frequently diagnostic and prognostic biochemical marker of liver cell damage. Any damage to hepatocytes i.e inflammation, necrosis, degenerative disease causes release of certain enzymes into circulation such as alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), gamma glutamy trasferase ( $\gamma$ GT), lactate dehydrogenase (LDH).<sup>1</sup>

Cloves are dried unopened floral buds of an evergreen tree Syzygium aromaticum.<sup>2</sup> Initially cloves were established in Sri Lanka, but they were highly expensive. Later on, India also introduced them and its use was highly appreciated during Christmas as scent in houses and decorates the festival.<sup>3</sup> Cloves have antimicrobial, antiseptic, analgesic, anti-inflammatory, chemo preventive, hepatoprotective, neuroprotective, and platelet aggregation inhibition effects.<sup>4</sup> The pathogenesis involved in drug induced hepatotoxicity is either dose dependent direct hepatotoxic effects such as paracetamol or idiosyncratic effects due to the

participation of a toxic drug or metabolite that either elicit the immune response or alters the biochemistry of cell. The drug metabolites can be electrophilic chemicals or free radicals that cause a chemical reaction such as depletion of reduced glutathione, covalently binds to lipids, proteins and nucleic acids or induces the lipid peroxidation, thus directly influences the cellular organelles. Activation and inhibition of signaling kinases, transcription factors and gene expression profiles indirectly affects the cellular organelles. The resultant intracellular stress leads to cellular death either by apoptosis or necrosis.<sup>5</sup> Herbs are the natural drugs that regain the alterations made in normal physiology of body by foreign organism or malfunctioning of the body.<sup>6</sup> Herbal medicines are in great demand in developed and undeveloped countries because of medicinal use, higher safety and lesser costs.<sup>7</sup> The amount of volatile and non volatile components identified in bud and leaf oil of syzygium aromaticum varies according to climatic conditions. The most dominated volatile constituents in bud oil are eugenol, eugenyl acetate and  $\beta$  caryophyllene, while harvested leaf oil is dominated by eugenol and  $\beta$  caryophyllene. The non volatile components of syzygium aromaticum are tannins, sterols, flavnoids and triterpins.<sup>8</sup> This study was conducted to determine the effects of Syzygium Aromaticum on liver enzymes.

1. Department of Pharmacology, Isra University Hyderabad, Pakistan.

### Correspondence:

Dr. Sadia Kazi, Department o Pharmacology, Isra University Hyderabad, Pakistan

E-mail: sadia\_kaq@hotmail.com

Received: 29-0316

Accepted: 03-05-2016

## METHODOLOGY

This was randomized control trial, 30 male and female rabbits weighting 2kgs on average were used in this study. All animals were acclimatized for few days before the start of experimental work. Animals were divided into three equal groups and were kept in separate cages under constant environmental conditions. All animals were fed with same diet and water. Approval was taken from the ethical committee before start of study. Paracetamol 500mg tablets were purchased from medical store of Isra University. Dried clove buds were purchased from local market of Hyderabad. It was grinded into fine powder by mechanical grinder and was stored in air tight container. The study was carried out at animal house of Tandojam Agriculture University and Postgraduate Laboratory Department of Pharmacology, Isra University. Duration of study was 3 months from 1<sup>st</sup> October to 31<sup>st</sup> December 2013. Healthy rabbits weighting 2kg on average of both genders were included. Rabbits < 1 kg in weight and rabbits > 2.5kgs in weight and Lactating Animals were excluded from the study. Hepatotoxicity was induced by paracetamol 500mg BD. 30 rabbits were randomly categorized into three groups, Group A control group, Group B was given paracetamol 500mg BD by feeding tubes for 10 Days, followed by powder syzygium aromaticum 100mg BD in water for next 10 days, Group C was given paracetamol 500mg BD and powder syzygium Aromaticum 100mg BD simultaneously in water by feeding tube for 10 days.

### Data Collection Procedure:

Rabbits were wrapped into towel and blood samples was collected from all 3 groups from the ear lobule of rabbits by 23 gauge butterfly cannula. Collected blood samples were biochemically analyzed for serum levels of Alanine transaminase (AST), Aspartate transaminases (AST), Alkaline Phosphatase (ALP), Gamma Glutamyl Transferase ( $\gamma$ -GT) and Lactate Dehydrogenase (LDH) on day 1<sup>st</sup> and 10<sup>th</sup> from all 3 groups and on day 20<sup>th</sup> from group B only by an automatic analyzer at laboratory of Isra University Hospital. Mean and standard deviation was calculated for numerical data and p-value <0.05 considered significant. The data was entered and analyzed by using SPSS version 16.

## RESULTS

These results show that the levels of all hepatic enzymes elevated with the paracetamol in group B in initial 10 days but subsequently declined with *Syzygium aromaticum* administration in next 10 days the p-value remained highly significant 0.001. There was no significant rise in these enzymes in group C which was co administered *Syzygium aromaticum* with paracetamol.

**Table I: Changes in Anzyme levels during study period.**

ENZYME	Group	Day 01	Day 10	Day 20	P-value
Alanine Transaminase (AST)	A	38.49±13.50	37.62±12.29		
	B	31.49±12.30	81.72±12.15	39.63±12.58	0.001
	C	39.39±11.22	42.32±11.58		
Aspartate Transaminase	A	33.79±5.81	33.02±4.52		
	B	25.89±10.29	67.42±14.80	35.03±11.34	0.001
	C	26.79±5.48	30.52±5.23		
Alkaline Phosphatase	A	175.95±41.93	177.32±47.78		
	B	173.85±46.1	290±30.75	203.64±42.82	0.001
	C	170.35±32.43	219.92±44.84		
Gamma Glutamyl Transferases	A	30.05±13.29	30.43±13.01		
	B	36.21±9.35	83.23±12.62	45.13±10.80	0.001
	C	41.01±11.99	47.23±11.40		
Lactate Dehydrogenases	A	376.59±73.62	384.83±65.87		
	B	434.29±95.77	851.33±92.78	489.14±91	0.001
	C	498.79±57.57	562.03±60.68		

## DISCUSSION

The results of the current study showed elevation of the plasma liver enzymes showing hepatotoxicity due to paracetamol. Results also showed that these elevated enzyme levels were declined by the *Syzygium aromaticum* (clove). These results were in accordance with the previous study by Abdel Wahaab et al on 60 sexually mature male Sprague drawley rats.<sup>9</sup> The study aimed to evaluate the Antioxidant property of *Nigella sativa* (black cumin) and *Syzygium aromaticum* (clove) in rats during aflatoxicosis and proved that *nigella sativa* and *syzygium aromaticum* oils succeeded in restoration of serum liver enzyme levels of ALT, AST and ALP towards normal values of control. The protective activity of *nigella sativa* oil may be due radical scavenging activity of its components while the beneficial effects of *syzygium aromaticum* oil may be due to presence of phenolic compound present in its oil.

ALT produced by hepatocytes thus it is most sensitive marker of hepatocellular injury. It is used as prognostic marker for identifying drug induced liver injury.<sup>10</sup> Its levels were raised in current study following paracetamol over dose and then declined by the effects of the *Syzygium aromaticum*. AST found in two iso-enzymes. Mitochondrial iso-enzyme is produced by hepatocytes and shows hepatocellular injury while cytosolic iso-enzymes is skeletal muscles, heart muscles and kidney tissues.<sup>11</sup>

Its levels were improved in our study suggesting recovery from hepatocellular injury.

ALP it occurs in group of iso-enzymes that dephosphorylate a number of molecules throughout the body. It is produced by membranes of cells lining bile ducts and canaliculi. Non hepatic productions are by kidneys, intestine, leucocytes, placenta and bones. Physiological rise occurs in pregnancy and growing children while pathological rise occurs in cholestatic, renal, Paget's diseases and bony metastasis.<sup>11</sup>

Gama GT it is produced by liver microsomes and biliary epithelial cells. Non hepatic productions are kidney, pancreas and intestine.<sup>11</sup> Elevation of  $\gamma$ GT along with ALT is highly suggestive of biliary tract obstruction. Lactate dehydrogenase is used in the diagnosis and treatment of liver diseases such as acute viral hepatitis, cirrhosis and metastatic carcinoma of liver, cardiac diseases such as myocardial infarction, and tumors of lungs and kidneys. Segeay, OE et al conducted experimental study of antioxidant and hepatoprotective effect of clove and cardamom in ethanol induced hepatotoxicity. The study proved that administration of cloves at dose of 500mg/kg and cardamom at dose of 500mg/kg succeeded in decreasing liver function enzyme levels of ALT, AST, ALP and GGT.<sup>12</sup> The study revealed the presence of antioxidant in clove and cardamom which possess phenolic compounds that act as free radical scavengers. The finding of lowering effect of hepatotoxicity by *Syzygium aromaticum* is consistent with present study and Sadeek EA et al proved the Chemo-protective effect of Turmeric, Chili, Cloves and Cardamom on Correcting Iron Overload-Induced Liver Injury, Oxidative Stress and Serum Lipid Profile in Rat Models.<sup>13</sup> These studies have significantly decreased serum liver enzymes levels towards the control values.

## CONCLUSION

*Syzygium aromaticum* is a hepatoprotective agent in paracetamol induced hepatotoxicity. We recommend further studies for isolation of different components of *Syzygium aromaticum* (clove) and their individual effects. We also recommend studies of this compound as an adjuvant therapy with interferon therapy for hepatitis C to observe for any potential beneficial effects. Studies comparing *Syzygium aromaticum* with N-Acetyl cysteine are also recommended.

## Conflict of interest

The authors have declared no conflict of interest.

## REFERENCES

1. Krier. M, Ahmed. A. The Asymptomatic Outpatient with Abnormal Liver Function Tests. *Clinical Liver Diseases*. 2009;13: 167-177.
2. Prasad. R.C, Herzog.B, Boone. B, Sims. L, Waltner-Law. M. An extract of *Syzygium aromaticum* represses genes encoding hepatic gluconeogenic enzymes. *Journal of Ethnopharmacology*. 2005;96: 295–301.
3. Miliand. P, Deepa. K. Clove: A Champion Spice. *International Journal of Research Ayurveda and Pharmacy*. 2011;2(1): 47-54.
4. Han. A. R, Paik. Y. S. Antioxidant and Prolyl Endopeptidase Inhibitory Capacities of Chromone C-glucosides from the Clove Buds (*Syzygium aromaticum*); *J Appl Biol Chem*. 2012; 55(3):195–198.
5. Kaplowitz, N. Drug-Induced Liver Injury. *Clinical Infectious Diseases*. (2004;38(2): 44–48.
6. Maaz. A, Bhatti.A. S. A, Maryam. S, Afzal. S, Ahmad. M, Gilan. I. A. N. Hepatoprotective Evaluation of *Butea monosperma* against Liver damage by Paracetamol in Rabbits. *Special Edition Annals*.2010;16:73-76.
7. Kshirsagar. A. D, Mohite. R, Aggrawala. S, Suralkar UR. Hepatoprotective Medicinal Plants Of Ayurveda—A Review. *Asian Journal Pharmacology Clinical Research*. 2011; 4(3): 1-8.
8. Pino JA, Marbot R, Aguero J, Fuentes. V Essential Oil from Buds and Leaves of Clove (*Syzygium aromaticum* (L.) Merr. et Perry) Grown in Cuba. *Journal of Essential Oil Research*. 2011;13(4):278-279.
9. Abdel-Wahab. MA, Aly S E. Antioxidant property of *Nigella sativa* (black cumin) and *Syzygium aromaticum* (clove) in rats during aflatoxicosis. *Journal of Applied Toxicology*. 2005; 25: 218–223.
10. M'Kada H, Munteanu M, Perazzo H, Ngo Y, Ramanujam N, Imbert-Bismut F, Ratzu V, et al. The Dili Group Of The Safe-Tconsortium. What are the best reference values for a normal serum alanine transaminase activity (ALT)? Impact on the presumed prevalence of drug induced liver injury (DILI). *Regulatory Toxicology and Pharmacology*. 2011;60: 290–295.
11. Hall P, Cash J. What is the Real Function of the Liver 'Function' Tests? *Ulster Medical Journal*. 2012;81(1):30-36.

12. Segacy O E, Ahmed AB Allah, Saad Abu Al Noman. Experimental study of antioxidant and hepatoprotective effects of Clove and Cardamom in ethanol induced hepatotoxicity. Tanta medical sciences. Journal. 2007;2: 27-36.
13. Sadeek E A, Fatimah , Abdel-Razek. The Chemo-Protective Effect of Turmeric, Chili, Cloves and Cardamom on Correcting Iron Overload-Induced Liver Injury, Oxidative Stress and Serum Lipid Profile in Rat Models. Journal of American Science.2010;6 (10): 702-712.

## Corrigendum

**Following are the corrections in**  
JSZMC; Vol.06, No.02, April-Jun 2015  
Page Number 794

**Dr. Hafiz Muhammad Yar<sup>1</sup>**

Department of Community Medicine, Sheikh Zayed Medical College/Hospital,  
Rahim Yar Khan.

**Dr. Huda Abbas<sup>2</sup>**: Department of Community Medicine, Quaid-e-Azam Medical  
College, Bahawalpur

**Dr. Muhammad Naeem<sup>3</sup>**: Department of Paediatric Medicine, Quaid-e-Azam  
Medical College, Bahawalpur

**Dr. Wajahat Hussain<sup>2</sup>**: Department of Community Medicine, Quaid-e-Azam  
Medical College, Bahawalpur