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EVALUATION OF HEPATOPROTECTIVE ACTIVITY OF AYA BRINGARAJA KARPAM, A HERBO METALLIC SIDDHA FORMULATION BY USING ZEBRA FISH MODEL

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ABSTRACT

Liver plays a vital role in detoxifying toxins from the blood, restoring energy and nutrients, digesting fats and processing food and medications in our body.Genetic factors, obesity, viruses, alcohol consumption and chronic usage of medications such as Anti-psychotic drugs, Analgesics, Anabolic steroids and oral contraceptives are some of the common factors causing liver diseases. Untreated liver diseases may also results in Liver Cirrhosis which is a life threatening condition. In Siddha system of medicine, there are numerous formulations with hepato protective activity. Aya Bringaraja Karpam is a popular and unique Siddha formulation with rejuvenative property commonly used in the management of Iron deficiency anemia, Jaundice and greying of hair. Aim The study is aimed to assess the hepato protective activity of Aya Bringaraja Karpam (ABK). Materials and Method The study drug purchased from SKM Siddha and Ayurvedha Pharmacy, Erode, Tamilnadu and hepato protective activity study was performed by paracetamol induced Liver dysfunction in Zebra fish Danio rerio model. The study was conducted in 4 groups with 10 adult Zebra fish each. Group I was treated as control, Group II treated as disease control group, Group III and IV received test drug ABK at the low and high doses respectively. Histo pathological assessment was done on the liver specimens of Zebra fish after 7 days exposure period. Results :The result revealed that paracetamol treated groups shows severe liver degeneration whereas treatment with test drug ABK at both the dose level of 250 and 500 mg/liter significantly attenuated the paracetamol induced Hepatotoxicity. This present study confirms the hepato protective effect of Aya Bringaraja Karpam against paracetamol induced liver damage in zebra fish model and it can be used for the management of liver diseases.

KEY WORDS: ***Siddha medicine, Aya Bringaraja Karpam, Hepato protective, Zebra fish***

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1. Introduction

The liver is considered as the most important organ which carries out many metabolic functions, providing the energy needed by the body. It plays an important role in metabolism, storage, protein synthesis and detoxification. More than 900 drugs have been reported to cause liver diseases such as acute dose dependent liver damage, acute fatty infiltration, cholestatic jaundice, liver granulomas, active chronic hepatitis, liver cirrhosis, liver tumors, etc. [1],

Acetaminophen also known as paracetamol, a widely used analgesic and antipyretic drug, can cause serious liver damage and even acute liver failure if it is taken in high doses and the recent studies revealed that consumption of paracetamol for longer duration is one of the leading causes of liver failure in the United States[2]. Several newly developed drugs such as rimonabant, propylthiouracil, or corticosteroids have been used in the management of liver diseases but these drugs possess harmful adverse effects such as insomnia, vomiting, constipation and depression [3]. To overcome this problem, scientific research on indigenous medicinal herbs and drug formulation is essential. Siddha system of medicine have been extensively used in the management of liver diseases due to its safety, efficacy and cost effectiveness.

Aya Bringaraja Karpam is a commonly used Herbo metallic Siddha formulation in the management of common liver diseases which is mentioned in the classical text “Siddha Vaidya Thirattu”.

Paracetamol is metabolized in the liver and it is converted to a metabolite called N- acetyl-P-benzo-quinone imine (NAPQI) which is toxic to hepatocytes. Overdose of paracetamol leads to ‘Paracetamol hepatotoxicity’ which causes signs of liver failure such as low blood sugar, low blood pH, easy bleeding and hepatic encephalopathy [4].

The tri-lobed liver of the zebra fish is similar to that of the mammal with regard to biological function, including the processing of lipids, vitamins, proteins and carbohydrates, as well as the synthesis of serum proteins. The zebra fish liver develops histological patterns of injury comparable to those of mammalian liver following exposure to a range of hepatotoxic drugs and biomarkers for liver injury can be quantified in the zebra fish circulation. Hence the zebra fish is a good alternative for in vivo studies due to its small size, genetics background, higher breeding capabilities, and the similarities of its molecular pathways and physiology with that of humans [5].

2. Materials and Methods

2.1 *Aya Bringaraja* Karpam [7-8]

The test drug *Aya Bringaraja Karpam* has been purchased from SKM Siddha and Ayurvedha Pharmacy, Erode, Tamilnadu. It is a herbo metallic Siddha formulation prepared from purified iron filings, purified dross iron, Eclipta and lime extracts which is indicated for Iron deficiency anemia, Jaundice and greying of hair. It is an effective rejuvenating Siddha drug**.**

Table 1. Ingredients of *Aya Bringaraja Karpam*

S.N	Siddha Name	Common Name	Quantity
1	Suthi seitha Ayapodi	Purified iron filings	140 grams
2	Suthi seitha Mandooram	Purified dross iron	210 grams
3	Karisalai saru	Eclipta juice	1.5 litre
4	Elumicham pasha saru	Lime juice	1.5 litre

2.2 Animal [9]

Adult Zebra Fish (*Danio rerio*) were purchased from the local supplier and were maintained in a laboratory condition 28 °C $\pm$ 1°C and a period of 14:10 h light/dark cycle photo period. All fishes’ were acclimatized to lab condition four weeks prior to the start of experimentation. Animals were divided in to four groups of 10 fish each.

Grouping

Group I – Control

Group II- Paracetamol 5mM (755.8mg) per liter concentration

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Group III- Paracetamol 5mM + ABK Low Dose 250 mg/liter
Group IV- Paracetamol 5mM + ABK High Dose 500 mg/liter

2.3 Treatment

Animal belongs to group I left untreated and group II treated with Paracetamol at the concentration of 5mM (755.8mg) per liter concentration for the period of seven days. Animal belongs to group III received test drug ABK at the concentration of 250 mg/liter and group IV received test drug ABK at the concentration of 500 mg/liter along with paracetamol 5mM for the period of seven days.

2.4 Histopathology

After a one-week exposure period, the liver of zebra fish were dissected and fixed in 10% formalin for 24 hours. Subsequently, the fixed liver tissues were dehydrated in gradient ethanol, hyalinized in xylene, and embedded in paraffin wax at 56 °C. Then, the paraffin blocks were sectioned at 5-µm thickness. The sections were collected on glass slides and stained with hematoxylin and eosin (H&E) using an H&E Staining Kit. Histologic lesions were observed using an optical microscope equipped with a digital camera.

3. Results and Discussion

The results of the present investigation indicates that paracetamol treated groups shows severe liver degeneration whereas treatment with test drug ABK at both the dose level of 250 and 500 mg/litre significantly attenuated the paracetamol induced damage in group III and IV.

In the present study, the histopathological studies were carried out using Light microscopy to check the hepatoprotective effect of *Aya bringaraja karpam* on paracetamol induced liver damage.

The H&E staining of the liver tissue of paracetamol and post treated group as shown in Figure 1.

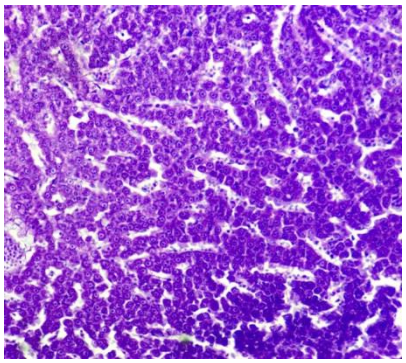

Figure 1: Histology of Control group

Figure 1 shows the control group with normal liver morphology with normal liver cells i.e., regular arrangement of hepatocytes with perfect cyto architecture.

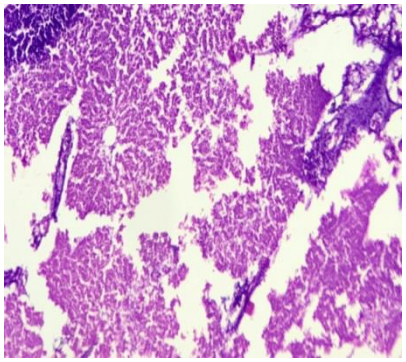

Figure 2: Histology of Paracetamol treated group

Paracetamol treated group shows the degeneration of vacuoles in the cell, increased sinusoidal space shrinkage in the size of the hepatocytes and necrotic aggregation of cells.

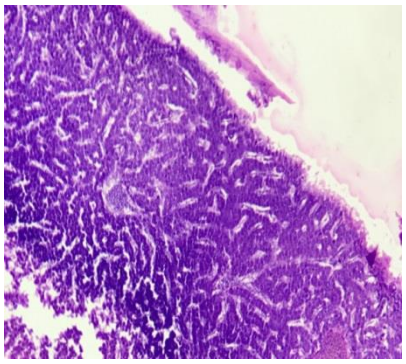

Figure 3: Histology of ABK 250 mg treated group

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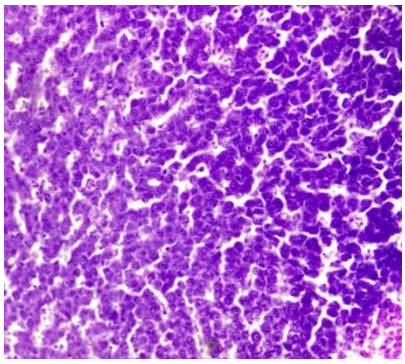

Figure 4: Histology of ABK 500 mg treated group

Figure 3 and 4 shows the post treatment with *Aya bringaraja karpam* of which group III reveals partial degeneration with evidence of improvement in cellular morphology and group IV reveals almost normal morphology and with regular sinusoidal space and regeneration of vacuoles, with no necrotic zone.

4. Conclusion

This study concluded that the test drug *Aya bringaraja karpam* possess promising hepatoprotective effect in dose dependent manners and restores the basic liver architecture by means of its rejuvenating potential and also ameliorated the degenerative changes induced by paracetamol in zebra fish model. It can be considered as a drug of choice for the management of liver diseases.

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