Hepatoprotective Effects of Thymus and *Salvia* Essential oils on Paracetamol-Induced Toxicity in Rats

By

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Abstract

Medicinal plants have been used traditionally worldwide for the prevention and treatment of liver disease. *Thymus Capitatus* and *Salvia Officinalis* are used frequently as spices. The present investigation aimed to investigate the possible potential protective effect of Thymus and *Salvia* essential oils against Paracetamol induced hepatotoxicity. Administration of Paracetamol (500 mg/kg.b.wt) resulted in liver damage as manifested by significant increase in serum and hepatic lactate dehydrogenase (LDH) activity with a significant decrease in blood and hepatic glutathione (GSH) levels, as well as blood and hepatic superoxide dismutase (SOD), and glutathione peroxidase (GPx) activities.

Rats pretreated orally with essential oil of *Thymus Capitatus* and *Salvia Officinalis* (50 mg/kg b. wt. daily) for 15 days then intoxicated with paracetamol showed a significant protection against-induced increase in serum and hepatic LDH activities and inhibit reduce GSH levels and enhance increase SOD and GPx activities in blood and liver.

These data indicate that essential oils of *Thymus Capitatus* and *Salvia Officinalis* possessed a hepatoprotective activity against hepatotoxicity induced by paracetamol model due to their antioxidant activity.

Key Words: Thymus Capitatus - Salvia Officinalis - hepatoprotective - antioxidant

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INTRODUCTION

Liver is a major site of metabolism and excretion. It is continuously exposed to xenobiotics which result in a variety of serious liver disorders. Plant based formulations are frequently employed for the liver diseases, but there are few effective suitable drugs available (Chatterjee, 2000). Therefore, many plant products have been evaluated for their possible antioxidant and hepatoprotective effects which might make them suitable for treatment chemical-induced liver damage in experimental animals. Phenolic compounds, are widely distributed in medicinal plants, spices, vegetables, fruits, grains, pulses and other seeds are an important group of natural antioxidants with possible beneficial effects on human health. They can participate in protection against the harmful action of reactive oxygen free radicals, which are involved in the development of most chronic degenerative diseases such as cardiovascular diseases and cancer (Block, et. al., 1992). These reactive oxygen metabolites can also be regarded as central players in the pathophysiology of the gastrointestinal tract (Koutouras, et. al., 2001).

Sage (Salvia Officinalis) is commonly used as a culinary herb. It is listed by the Council of Europe as a natural source of food flavoring. Sage is stated to possess carminative, antispasmodic, antiseptic, and astringent properties. Traditionally, it has been used to treat flatulent dyspepsia, pharyngitis, uvulitis, gingivitis, glossitis (internally or as a gargle/mouthwash), hyperhidrosis, and galactorrhoea. The herbals of Gerard, Culpeper and Hill credit sage with the ability to enhance memory (Perry, 1984). The approved internal use for dyspeptic symptoms and excessive perspiration, and external use for inflammation of mucous membranes of mouth and throat. Many Salvia species and their isolated constituents possess significant antioxidant activity in enzyme-dependent and enzyme-independent systems (Dorman et al., 1995; Hohmann et al., 1999; Lu and Foo, 2001; Malencic et al., 2000; Zupko et al., 2001).

Thyme Thymus Capitatus is stated to possess carminative, antispasmodic, antitussive, expectorant, secretomotor, bactericidal, anthelmintic and astringent properties. Traditionally, it has been used for dyspepsia, chronic gastritis, asthma, diarrhoea in children, enuresis in children, laryngitis, tonsillitis (as a gargle), and specifically for bronchitis. The German Commission E approved internal use for treating symptoms of bronchitis, whooping cough and catarrh of the upper respiratory tract. Thyme is used in various combinations with anise oil, eucalyptus oil, fennel oil, fennel fruit, Iceland moss,
liquorice root, marshmallow root, primrose root and star anise fruit for catarrh and diseases of the upper respiratory tract (Opdyke 1974).

The present investigation aimed to investigate the possible potential hepatoprotective effect of *Thymus Capitatus* and *Salvia Officinalis* essential oils, against paracetamol induced hepatotoxicity in rats.

**MATERIALS AND METHODS**

2.1. Plant material

The selected plants were collected and taxonomic identifications were established by the staff members of the Department of Flora, Faculty of science, Cairo University. Sample was kept in the Department of Pharmacology, Faculty of Veterinary Medicine, Cairo University, Egypt. The air dried plant material (250 g) was pulverized, and stored for further use.

**Essential oils** of *Thymus Capitatus* and *Salvia* was prepared by steam distillation as described by (Ivanic and Savin 1976).

2.2. Paracetamol was provided by Medizen Company (Alexandria, Egypt). When intended to be used in vivo experiments, paracetamol was suspended in 0.5 % tween 80 and orally administrated in dose of 500 mg/kg. body weight. (Kostrubsky et al., 1995).

2.3. Animals

Adult albino rats weighing around 180-200 gm were purchased from Faculty of Veterinary Medicine, Cairo University. They were acclimatized to animal house conditions. Animals were provided with standard diet and water ad libitum. Rats were kept under constant environmental condition and observed daily throughout the experimental work. The study was approved with the Committee for the purpose of control and supervision of experimental animals in Faculty of Veterinary Medicine (FVM), Cairo University and the registration of FVM guidelines were followed for animal handling and treatment.

**Experimental Set Up:**

The animals were divided into seven groups with seven animals in each.

**Group I:** control healthy (was given similar volume of 0.5% tween 80).

**Group II:** Was given paracetamol (500 mg/kg b.wt. in 0.5% tween 80) in a single daily dose for the last 5 days of the experimental period (Kostrubsky et al., 1995).

**Group III:** Was treated with *Salvia* essential oil (50 mg/kg b.wt.) suspended in 0.5% tween 80 orally in a single daily dose for 15 days.
**Group IV:** Was pretreated with *Saliva* essential oil (50 mg/kg b.w.) alone for 10 days then received both *Saliva* essential oil (50 mg/kg b.w.) and paracetamol (500 mg/kg b.w.) for other 5 days.

**Group V:** Was pretreated with *Thymus* oil (50 mg/kg b.wt.) alone for 15 days.

**Group VI:** Was pretreated with *Thymus* oil (50 mg/kg b.wt.) alone for 10 days then received both *Thymus* oil (50 mg/kg b.wt.) and paracetamol (500 mg/kg b.wt.) for other 5 days.

**Group VII:** Was pretreated with was used as a standard group and received silymarin orally at a dose of 100 mg/kg b.wt. alone for 10 days then received both silymarin (100mg/kg b.w.) and paracetamol (500 mg/kg b.w.) for other 5 days.

**Treatment of Blood Samples**

After 15 days of treatment blood samples were withdrawn from the retro-orbital vein of each animal and each sample was collected into 2 tubes, heparinized and non-heparinized. The non-heparinized blood samples were allowed to coagulate and then centrifuged at 1000 xg for 20 min. The separated sera were used for the estimation of serum activity of LDH and TBARS, Pr-SHs, total protein levels. The heparinized blood samples were divided into 2 aliquots. The first aliquot was used for determination of GPx activity. The second aliquot was haemolyzed using bidistilled water and the haemolysate of each sample was divided into two portions. The first portion was treated with chloroform/ethanol (3:5 V/V) mixture to precipitate and the resultant supernatant was used for the determination of SOD activity. The second portion was deproteinized with metaphosphoric acid and the clear supernatant was used for the estimation of GSH level. Haemoglobin levels were determined in the heparinized blood samples and used in the calculation of the enzyme activity.

**II-Preparation of Liver Samples:**

Animals were sacrificed by cervical dislocation, and the livers were rapidly removed. A part of each liver was weighed and homogenized, with ice-cooled saline to prepare 5% W/V homogenate. The homogenate was divided into two aliquots. The first one was deproteinized with ice-cooled 12% trichloroacetic acid and the obtained supernatant, after centrifugation at 1000 xg, was used for the estimation of GSH. The second aliquot was centrifuged at 1000 xg and the resultant supernatant was used for estimation of lactate dehydrogenase (LDH), lipid peroxides (TBARS), and protein thiols (Pr-SHs).
Serum analysis

Determination of serum and hepatic LDH, TBARS, Pr-SHs and GSH levels in blood and hepatic were determined by the methods described by (Buhl and Jackson, 1978; Uchiyama and Mihara, 1987; Koster, et al., 1986 and Chanarin, 1989), respectively. The enzymatic determination of superoxide dismutase (SOD) activity according to method described by Nishikimi et al., (1972), glutathione peroxidase (GPx) activity according to method described by Paglia and Valentine (1967), alkaline phosphates activity (ALP) according to the method of Kind and king (1954), AST or ALT activity in serum according to the method of Reitman and Frankel (1957)

2.6. Statistical analysis

The data were expressed as mean± Standard deviation (SD). Differences between means in different groups were tested for significance using a one-way analysis of Variance (ANOVA) followed by Duncan’s multiple range tests. Differences were significant at level \( P<0.05 \) according to Snedecor and Cochran (1986) using SPSS program version 15.

RESULTS

Table 1 and 2 shows the concentration of serum and liver LDH, TBARS, and Pr-SHs of control and experimental groups of rats. Paracetamol (500 mg/kg.), orally given to rats markedly increased serum and hepatic LDH activity. Also, the levels of serum and hepatic TBARS in paracetamol treated rats were significantly higher than control rats, whereas rats-treated with Thymus or Salvia before paracetamol [ (group 4) (group 6)] restored the altered values to the near normal values. The decreased concentration of serum and hepatic Pr-SHs was observed in paracetamol intoxicated rats. Administration of Thymus or Salvia before paracetamol groups tends to bring the Pr-SHs level to near normal. Table 3 shows the concentration of blood reduced glutathione (GSH), activities of Superoxide dismutase (SOD) and glutathione peroxidase (GPx) of control and experimental groups of rats. The decreased concentration of blood and hepatic GSH was observed in paracetamol control rats. Administration of Thymus or Salvia groups tends to bring the GSH level to near normal.

The effect of essential oils of Thymus or Salvia at dose of 50 mg/kg b.wt on liver enzymes (ALT, AST, and ALP) was reported in Table (4). Paracetamol elevated the ALT, AST and ALP level in the intoxicated group as compared to those of the control (non treated) group. Rats pretreated with essential oils of Thymus or Salvia at dose of 50 mg/kg b.wt for 15 days significantly protected the liver and decreased the ALT, AST and
ALP as compared to paracetamol intoxicated group. Silymarin significantly decreased the enzyme activity.

**DISCUSSION**

The present study was conducted to evaluate the beneficial effects of essential oils of *Thymus* or *Salvia* and antioxidant status in paracetamol-induced hepatotoxicity rats. The preliminary studies conducted by this work revealed the nontoxic nature of *Thymus* or *Salvia* on normal rats. Paracetamol causes acute centrilobular hepatic necrosis in rats and other animal species (*Piperno et al.*, 1978). Hepatic necrosis following massive paracetamol administration is well documented (*Waters et al.*, 2001). Drastic elevation in the activity of serum and liver cytosolic LDH were shown in the current study after administration of paracetamol (500 mg/kg.b.w). Paracetamol toxicity was reported to associate with increased released of LDH in experimental animals (*Blazka et al.*, 1996). Increase in cytosolic LDH activity by paracetamol might be due to the intracellular accumulation of Ca2+, which results in activation of phosphofructokinase and anaerobic glycolysis leading to lactate formation (*Landowne and Ritchie*, 1971). Loss of Ca2+ homeostasis as a result of oxidative damage and increase in intracellular Ca2+ has been reported to a late and perhaps irreversible final stage in the process of cell death for paracetamol (*Strubelt and Younes*, 1992). *Salvia Officinalis* and *Thymus Capitatus* administration controlled serum and hepatic LDH. However, it did not normalize the LDH level completely as it remained lesser than paracetamol treated rats.

There is a growing interest in the antioxidant properties of many herbs and spices that were reported to be effective in retarding the process of lipid peroxidation in oils and fatty acids (*Namiki, 1990, Pokorny, 1991, Duh and Yen, 1997*). The antioxidant activity of essential oils of *Thymus Capitatus* or *Salvia Officinalis* was proven by a significant increase in the levels of all the antioxidant enzymes (GSH and SOD) in liver homogenates in rats. In this concern, (*Grigore1, et al., 2010*) reported that Volatile oil obtained by steam distillation of Thymus contains high amounts of thymol and p-cymene which had potent antioxidant effect, indicated by significant increase of superoxide anions, and lipid oxygen radicals due to lipid peroxidation as proven in this study. In addition, *Miura, et. al., (2002)* reported that a new abietane diterpenoid, together with 1 anthraquinone, and 8 flavonoids, was isolated from the leaves of *Salvia Officinalis*. *Muriel and Mourelle (1990)* stated that flavonoids interacts directly with the cell membrane components to prevent any abnormalities in the content of lipid fraction, which is responsible for maintaining normal fluidity. Several investigators previously reported the potent *in vivo* antioxidant activity of *Thymus* oil, *Grigore, et al. (2010)*, referred its
*in vivo* antioxidant activity via increasing the levels of glutathione, which is an important antioxidant that detoxifies an array of hormones, drugs and chemicals. Furthermore, Pradhan and Girish (2006) mentioned that glutathione enhancer and liver regenerator effects as the result obtained from this study. Concerning the antioxidant activities of *Salvia Officinalis*. It was found the plant extract had high free radical scavenger activity expressed as a reactive reaction % at a dose dependant manner. However, it was less potent than ascorbic acid activity. In this concern, (Miura, et. al., 2002) reported that flavonoids of *Salvia Officinalis* had potent antioxidant effect, capable of scavenging free radicals, superoxide anions, and lipid oxygen radicals due to lipid as proven in this study. Furthermore, Grzegorczyk, (2007) reported that, methanolic and acetone extracts from organ (shoots and hairy roots) and undifferentiated (cell and callus) cultures of *Salvia Officinalis*, as well as from shoots and roots of *in vitro* regenerated plants were evaluated for their antioxidant properties using three various *in vitro* models: scavenging of the free radicals using DPPH transition metal reduction in phosphomolybdenum assay and inhibition of lipid oxidation. The concentrations of rosmarinic acid, diterpenoids (carnosic acid and carnosol) and total phenolic compounds in each extract were determined. The methanolic hairy root and root regenerated plant extracts possessed the strongest effects on reducing Mo and DPPH* radical scavenging. On the other hand the best protective effect against linoleic acid oxidation was observed for acetone extracts of shoots obtained from *in vitro* culture followed by the extracts of shoots of intact plants grown in the field, without statistically significant differences between them.

In the present study, the elevation of GSH levels in blood and liver was observed in the treated rats with either *Thymus* or *Salvia* essential oils. This indicates that these plants can either increase the biosynthesis of GSH or reduce the oxidative stress leading to less degradation of GSH, or have both effects. SOD has been postulated as one of the most important enzymes in the enzymatic antioxidant defense system which catalyses the dismutation of superoxide radicals to produce H$_2$O$_2$ and molecular oxygen (Crod et al., 1976), hence diminishing the toxic effects caused by their radical.

**CONCLUSION**

In conclusion, our results demonstrated that essential oils of *Thymus* or *Salvia Officinalis* has a potent hepatoprotective and *in vivo* and *in vitro* antioxidant effects. The hepatoprotective effect of these oils may be due to the decreased liver enzyme levels with significant improvement to the histological picture of liver. The activity of antioxidant
enzymes are significantly increased in pretreated extract rat liver homogenate. Inhibition (\%) of reaction reactive rate by oils of Thymus or Salvia in vitro confirms that it is a potent free radical scavenger

REFERENCES
Grigore1, A, Paraschiv1,I ; Colceru-mihull1, S.; c. Bubueanu1, C.; Draghici1, E.; Ichim, M., 2010: Chemical composition and antioxidant activity of Thymus vulgaris L.volatile oil obtained by two different methods. Romanian Biotechnological Letters, 15, (4) 5436-5443,


Table (1): Effect of treatments on the levels of lactate dehydrogenase (LDH), lipid peroxides (TBARS), and protein thiols (Pr-SHs) in serum of rats (n=7).

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg b.wt.)</th>
<th>LDH (U/g protein)</th>
<th>TBARS (nmol/ml)</th>
<th>Pr-SHs (µmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Healthy</td>
<td>0.0</td>
<td>188.00±6.78c</td>
<td>2.47±0.17b</td>
<td>551.5± 4.76a</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>5 00 mg/kg b.w.</td>
<td>530.4±7.45a</td>
<td>7.85±0.46a</td>
<td>470.487±3.47b</td>
</tr>
<tr>
<td>Salvia Officinalis</td>
<td>50 mg/kg b.w.</td>
<td>164.7±4.21c</td>
<td>1.8±0.11c</td>
<td>580.74±2.41a</td>
</tr>
<tr>
<td>Salvia Officinalis + Paracetamol</td>
<td>50 mg/kg b.w. + 500 mg/kg b. wt</td>
<td>274.00±3.46b</td>
<td>3.2±0.21b</td>
<td>519.24±2.57b</td>
</tr>
<tr>
<td>Thymus Capitatus</td>
<td>50 mg/kg b.wt</td>
<td>156.8±2.57c</td>
<td>1.5±0.11c</td>
<td>595.0±3.57a</td>
</tr>
<tr>
<td>Thymus Capitatus + Paracetamol</td>
<td>50 mg/kg b.wt + 500 mg/kg b. wt</td>
<td>231.24±2.17b</td>
<td>2.9±0.006b</td>
<td>5.35.74 ±8.29a</td>
</tr>
<tr>
<td>Slimarin + Paracetamol</td>
<td>100 mg/kg + 500 mg/kg b. wt</td>
<td>216.24±2.17b</td>
<td>2.8±0.006b</td>
<td>580.4±1.58a</td>
</tr>
</tbody>
</table>

Values within a column with no common superscript letters are significantly different (P ≥ 0.05).
Table (2): Effect of treatments on the activity of lactate dehydrogenase (LDH) and levels of lipid peroxides (TBARS) and protein thiols (Pr-SHs) in liver of rats (n=7)

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg b.wt.)</th>
<th>LDH (U/g protein)</th>
<th>TBARS(nmol/ml)</th>
<th>Pr-SHs(µmol/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Healthy</td>
<td>0.0</td>
<td>308.2±2.57&lt;sup&gt;b&lt;/sup&gt;</td>
<td>268.2±1.58&lt;sup&gt;b&lt;/sup&gt;</td>
<td>75.7±1.39&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>5 00 mg/kg b.w.</td>
<td>760.42±3.16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>785.54±2.68&lt;sup&gt;a&lt;/sup&gt;</td>
<td>49.5±1.57&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Salvia Officinalis</em></td>
<td>50 mg/kg b.w.</td>
<td>270.5±3.36&lt;sup&gt;b&lt;/sup&gt;</td>
<td>185.7±2.36&lt;sup&gt;b&lt;/sup&gt;</td>
<td>84.2±2.39&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Salvia Officinalis</em> + Paracetamol</td>
<td>50 mg/kg b. wt + 500 mg/kg b. wt</td>
<td>335.47±2.68&lt;sup&gt;b&lt;/sup&gt;</td>
<td>295.3±1.27&lt;sup&gt;b&lt;/sup&gt;</td>
<td>89.4±3.48&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Thymus Capitatus</em></td>
<td>50 mg/kg b.wt</td>
<td>290.32±3.87&lt;sup&gt;b&lt;/sup&gt;</td>
<td>199.48±1.34&lt;sup&gt;b&lt;/sup&gt;</td>
<td>89.9±4.38&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>Thymus Capitatus</em> + Paracetamol</td>
<td>50 mg/kg b.wt + 500 mg/kg b. wt</td>
<td>320.38±1.58&lt;sup&gt;b&lt;/sup&gt;</td>
<td>279.65±2.76&lt;sup&gt;b&lt;/sup&gt;</td>
<td>86.2±2.38a</td>
</tr>
<tr>
<td>Slimarin + Paracetamol</td>
<td>100 mg/kg + 500 mg/kg b. wt</td>
<td>315.98±2.58&lt;sup&gt;b&lt;/sup&gt;</td>
<td>272.5±2.17&lt;sup&gt;b&lt;/sup&gt;</td>
<td>83.4±3.28&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values within a column with no common superscript letters are significantly different (P ≥ 0.05).
Table 3: Effect of treatments on the level of reduced glutathione (GSH) and activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx) in blood of rats (n=7).

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg b.wt.)</th>
<th>GSH(mg %)</th>
<th>SOD(U/g Hb)</th>
<th>GPx(U/g Hb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Healthy</td>
<td>0.0</td>
<td>55.2 ± 3.89 a</td>
<td>15.2 ± 2.37 a</td>
<td>161.5 ± 3.58 a</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>500 mg/kg b.w.</td>
<td>32.5 ±0.24 b</td>
<td>7.54±0.27 b</td>
<td>112.9± 1.47 b</td>
</tr>
<tr>
<td>Salvia Officinalis</td>
<td>50 mg/kg b.w.</td>
<td>70.5± 4.38 a</td>
<td>18.7± 0.57 a</td>
<td>120.4± 1.28 b</td>
</tr>
<tr>
<td>Salvia Officinalis + Paracetamol</td>
<td>50 mg/kg b.wt + 500 mg/kg b. wt</td>
<td>51.2±1.35 a</td>
<td>13.6±0.19 a</td>
<td>154.24 ± 1.21 a</td>
</tr>
<tr>
<td>Thymus Capitatus</td>
<td>50 mg/kg b.wt</td>
<td>62.3±1.1 a</td>
<td>19.9±1.28 a</td>
<td>148.7± 3.14 b</td>
</tr>
<tr>
<td>Thymus Capitatus + Paracetamol</td>
<td>50 mg/kg b.wt + 500 mg/kg b. wt</td>
<td>50.8. ± 0.24 a</td>
<td>16.4±0.14 a</td>
<td>157.2 ± 1.21 a</td>
</tr>
<tr>
<td>Slimarin + Paracetamol</td>
<td>100 mg/kg + 500 mg/kg b. wt</td>
<td>51.6± 0.37 a</td>
<td>16.2±0.12 a</td>
<td>159.24± 1.17 a</td>
</tr>
</tbody>
</table>

Values within a column with no common superscript letters are significantly different (P ≥ 0.05).
Table 4: Effect of treatments on the activity of AST, ALT and AIP in rats, (n=7).

<table>
<thead>
<tr>
<th>Group</th>
<th>Dose (mg/kg b.wt.)</th>
<th>ALT (U/ml)</th>
<th>AST (U/ml)</th>
<th>ALP(U/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Healthy</td>
<td>0.0</td>
<td>82.8±2.24a</td>
<td>133.4±1.96a</td>
<td>135.8±2.63a</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>5 00 mg/kg b.w.</td>
<td>124.4±5.00b</td>
<td>263.0±7.68b</td>
<td>229.4±1.91b</td>
</tr>
<tr>
<td><em>Salvia Officinalis</em></td>
<td>50 mg/kg b.w.</td>
<td>76.8±4.16a</td>
<td>148.0±4.96a</td>
<td>127.6±1.58a</td>
</tr>
<tr>
<td><em>Salvia Officinalis</em> + Paracetamol</td>
<td>50 mg/kg b. wt + 500 mg/kg b. wt</td>
<td>79.4±4.62a</td>
<td>139.2±2.59a</td>
<td>136.6±2.87a</td>
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<tr>
<td><em>Thymus Capitatus</em></td>
<td>50 mg/kg b.wt</td>
<td>88.8±2.16a</td>
<td>141.6±5.79aa</td>
<td>128.4±3.76b</td>
</tr>
<tr>
<td><em>Thymus Capitatus</em> + Paracetamol</td>
<td>50 mg/kg b.wt + 500 mg/kg b. wt</td>
<td>86.5±1.94a</td>
<td>125.4±6.37a</td>
<td>142.8±3.42a</td>
</tr>
<tr>
<td>Slimarin + Paracetamol</td>
<td>100 mg/kg + 500 mg/kg b. wt</td>
<td>92.8±6.17b</td>
<td>126.4±5.21a</td>
<td>139.7±3.29a</td>
</tr>
</tbody>
</table>

Values within a column with no common superscript letters are significantly different (P ≥ 0.05).