ROLE OF α-TOCOPHEROL AND GINKGO BILOBA EXTRACT AS FREE RADICAL SCAVENGERS IN ENDOXTEN-INDUCED LIVER TOXICITY

Musheera Ibrahim, PhD1; Amal J. Fatani, PhD1; Fairouz E. Mohammed Ali, PhD2.
Pharmacology1 and Biochemistry2 Department, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

INTRODUCTION

The incidence of septic shock has increased progressively over the decades and represents a major cause of mortality in modern intensive care medicine (Friedman, 1998). It usually occurs in the young and old, or those suffering from several diseases such as diabetes, cancer, nephritis, and myocardial infarction (Klöfter, 1998). Septic shock is caused by an inadequate inflammatory and immunological host response to bacterial infection. In the Gram-negative bacteria, one of the most potent products in the induction of multiorgan failure and death is LPS (Grandel & Grimmingen, 2003). The dominant organ of LPS entrapment following its administration is the liver (Nettos & Roth, 1993). Gram-negative bacterial endotoxin-induced tissue injury may be due to release of a complex array of agents that can destroy normal cells as well as reactive oxygen species (ROS) (Daniela & Salvato, 2002). The ROS are known to injure tissue through peroxidation of membrane lipids, thus it is assumed that the resultant membrane damage can be prevented by antioxidants.

AIM OF THE WORK

Since antioxidants are capable of reducing the effects of free radicals formed in the body, thus the aim of this study was to elucidate the benefits of administration of a hypotoxic, α-tocopherol (α-TOC) and/or a naturally occurring antioxidant, extract of ginkgo biloba leaves (EGb 761), in minimizing the involvement of oxidative changes in experimental endotoxin-evoked liver toxicity.

RESULTS

Table 1: Survival rate in mice injected with LPS endotoxin alone or following pretreatment with α-tocopherol and/or EGb-761

<table>
<thead>
<tr>
<th>Animal Groups</th>
<th>After 24 hours</th>
<th>After 48 hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gr I (control)</td>
<td>100% (15/15)</td>
<td>100% (15/15)</td>
</tr>
<tr>
<td>Gr II (EGb 761, 150 mg/kg) pretreatment endotoxin injection</td>
<td>45.3% (7/15) **</td>
<td>33.3% (5/15) ***</td>
</tr>
<tr>
<td>Gr III (α-TOC, 100 mg/kg) pretreatment endotoxin injection</td>
<td>69.2% (10/15) **</td>
<td>48.0% (7/15) ***</td>
</tr>
<tr>
<td>Gr IV (α-TOC, 100 mg/kg) &amp; EGb 761 (150 mg/kg) pretreatment endotoxin injection</td>
<td>100% (15/15)</td>
<td>86.7% (13/15) **</td>
</tr>
</tbody>
</table>

The effectiveness of the antioxidant gingko biloba extract, alone or in combination with α-TOC, was the most significant in terms of liver function examination and histological study (Gr 7). Groups 3 & 5 are the treatments alone. Refer to methods for further details. At *, values are significantly different than control-treated group (*, P<0.05; **, P<0.001). At +, values are significantly different than LPS endotoxin-treated group (+, P<0.001).

Figure 3: Effect of pretreatment with α-tocopherol and/or ginkgo biloba extract (EGb-761) on hepatic malondialdehyde levels (MDA) in normal and endotoxemic rats.

Figure 4: Effect of pretreatment with α-tocopherol and/or ginkgo biloba extract (EGb-761) on hepatic glutathione reductase (GSH-R) and glutathione peroxidase (GSH-P) activities in normal and endotoxemic rats.

DISCUSSION

The effectiveness of the antioxidant ginkgo biloba extract, alone or in a greater degree in some instances when combined with aprotinin in ameliorating venom-evoked changes indicate the involvement of oxidative stress in venom-induced cellular damages seen in the rat heart and lungs.

CONCLUSION

The administration of α-tocopherol (α-TOC) and/or EGb 761 is reported to control the lipid peroxidation by reducing the liver damage in rats (P<0.001). The combined therapy provides complete protection against LPS-induced decrease in hepatic GSH-R and GSH-P activities.

MATERIALS AND METHODS

Male Wistar rats (n=15) were intraperitoneally injected with LPS (13 mg/kg) alone or in combination with α-tocopherol (α-TOC, 100 mg/kg) or the standardized extract of Ginkgo biloba leaves (EGb 761, 150 mg/kg). Separate control groups were injected with dilluents or selected treatments (α-TOC, EGb 761) alone. The percentage of survivals was calculated. All surviving rats were decapitated 18 hrs after the last injection and their livers removed quickly, weighed and minced. The organs were then homogenized in 0.5% iced trichloroacetic acid as 10% w/v homogenates using a glass Potter Elvehjem homogenizer. The homogenates were then centrifuged and the supernatants were used in the following assays:

- Glutathione reductase activity (GSH-R): method of Carlberg and Mannervik [1980];
- Glutathione peroxidase activity (GSH-P): method of Lawrence and Buck [1976];
- Malondialdehyde levels (MDA), as an index of lipid peroxidation: method of lichyama & Mihara [1978];
- Superoxide dismutase activity (SOD): method of Winterbourn et al. [1975];
- Liver homogenate protein content: method of Lowry et al. [1951];
- Statistical analysis: Statistical analysis was performed utilizing Fisher's exact test in survival analysis or Anova one way analysis and Tukey Kramer post tests in remaining experiments, with p-value 0.05 considered significant.

REFERENCES

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