Corriandrum sativum: Does it protect the mouse liver in paracetamol poisoning?

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Abstract

Acetamenophen (paracetamol) is one of the most commonly used and recommended non prescription analgesic and antipyretic medication. It is frequently consumed and its indiscriminate ingestion can lead to poisoning and potentially fatal hepatotoxicity.

Corriandrum sativum "Kottamalli", the commonly known medicinal plant is used against acute and chronic congestion of the liver and jaundice by the traditional medical practitioners in Sri Lanka. The objective of the present study is to evaluate the potency of Corriandrum against paracetamol induced hepatotoxicity in mice and to compare the effect with the known antidote, N-acetyl cysteine.

Twenty male, ICR mice (30-35 g body weight) were assigned to group. Hepatotoxicity was induced by the administration of a single oral dose of paracetamol (300 mg kg^{-1} in saline) after a 16 h fast. An aqueous extract of the whole plant (0.9 g/kg) was used on a pre and post-treatment basis. Pre-treatment with Corriandrum reduced the serum alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase by 42.41, 44.29 and 40.38 percent respectively while the post-treatment reduced the same by 48.27, 62.29 and 4.24 percent respectively. The reduced glutathione level was also increased in the plant treated groups but a significant improvement was observed only in the pre treated group, 4 h after the administration of paracetamol. A histopathological assessment of the liver damage was also conducted in parallel to the biochemical analysis. Histopathologically, an improvement in the liver cell architecture was observed in both treatment regimes, post treatment being better than the pre treatment. Although the extent of protection was not as good as N-acetyl cysteine, the known antidote, Corriandrum also protected the liver against paracetamol poisoning.

In paracetamol overdose, concentration of the toxic metabolite, N-acetyl parabenzo-quinone imine (NAPQI) increases, which can cause covalent binding, oxidative stress, lipid peroxidation and confluent necrosis in the liver.

Results from the present study indicated that under the present experimental conditions Corriandrum sativum possess a hepatoprotective and an antioxidative effect against paracetamol induced hepatotoxicity.

Keywords: *Corriandrum*, Hepatotoxicity, Paracetamol, Mice

Introduction

In the practice of traditional ayurvedic medicine in Sri Lanka, a number of herbs have been recognized for the potential benefits in the treatment of liver disorders. *Corriandrum sativum* Linn (Umbelliferae) commonly known as "Kottamalli" is found in Sri Lanka, India, Syria and Palestine. The seed of the plant is used by traditional medical practitioners as a diuretic and for catarrh, sore throat, hepatic derangements and as an aphrodisiac. (Jayaweera, 1981).

The present study was conducted to scientifically prove or disprove the therapeutic efficacy of *Corriandrum sativum* as a hepatoprotective agent against paracetamol (acetaminophen) induced hepatotoxicty. Paracetamol is one of the most widely used non-narcotic analgesic and antipyretic agents in the world, because of its overall efficacy and safety (Nelson, 1990). It is also frequently misused and its indiscriminate ingestion can lead to poisoning and potentially fatal hepatotoxicity (Black, 1984).

Management of paracetamol poisoning is still a major problem in developing countries as the drugs used for it are not readily available, expensive, ineffective or may cause adverse side effects. Therefore there is still a need to search for alternative drugs that would be effective, safe and inexpensive. Hepatoprotective drugs from plant sources seem to be an attractive alternative.

Materials and Methods

Paracetamol induced hepatotoxicity: Mice were randomly divided into six groups of 20 animals in each. The first group served as the normal control group and received distilled water orally. The second group was treated with the *Corriandrum* extract (0.9 g kg^{-1}, oral) for seven days. Animals were sacrificed seven days after the administration of the plant extract. 300 mg kg^{-1} of paracetamol was administered orally after a 16h fast. Third group was given paracetamol alone and they were sacrificed four hours later. Fourth group received the same dose of paracetamol and half an hour later N-acetyl cysteine (NAC) was given orally at 500 mg kg^{-1}. Mice were sacrificed 4 h later. In the fifth group *Corriandrum* extract was administered instead of N-acetyl cysteine. *Corriandrum* extract was administered for seven days in the sixth group and on the seventh day paracetamol was administered orally. Animals were sacrificed 4 h later.

Assessment of liver damage: Blood was drawn by cardiac puncture under ether anaesthesia to determine serum ALT, AST and ALP. Livers were excised, weighed and a section of the liver was fixed in 10% buffered formalin for histopathological assessment of liver damage. A liver section was homogenized and used for the determination of liver reduced glutathione (GSH) level. Serum ALT, AST and ALP activities were measured using an assay kit from Randox, UK. (Reitman & Frankel, 1957). Liver reduced glutathione level was estimated by the method of Jollow *et al* (1974). Histological sections of the formalin fixed liver tissue were stained with haematoxylin and eosin.
Statistical analysis: Results were expressed as mean ± SEM and all statistical comparisons were made by means of the One way Analysis of Variance. $P < 0.05$ was considered significant.

Results

As shown in Table 1, the activities of serum ALT, AST and ALP, 4 h after the administration of paracetamol alone were significantly increased ($P<0.001$). In addition, liver reduced glutathione levels were significantly decreased ($P<0.001$) compared to the normal control.

Corriandrum pre-treated mice 4 h after the administration of paracetamol also showed a significant decrease ($p<0.05$) in serum enzyme levels and a significant increase in the liver GSH (Table 1). Although the extent of protection was not as potent as N-acetyl cysteine, *Corriandrum* also proved to be an effective hepatotonic.

Table 1. Effect of *Corriandrum* extract on paracetamol induced hepatotoxicity in mice. n=20. Results indicated as mean ± SEM, ns-not significant. Level of significance p<0.05.

Treatment	ALT (U/l)	AST(U/l)	ALP(U/l)	GSH (μ/g liver)
Normal control	5.06 ±0.65	12.35 ±0.83	14.23 ±2.06	2916.04 ±22.4
Corriandrum control	5.82 ±0.63	15.10 ±1.31	15.64 ±1.71	2479.13 ±101.56
Paracetamol control 4h	588.12 ±38.62	609.37 ±60.10	89.58 ±7.14	346.16 ±64.59
NAC control 4h	13.0 ±1.69	30.625 ±5.61	47.49 ±4.96	3363.3 ±157.53
Corriandrum-post-4h	304.21* ±23.39	229.74* ±22.99	85.78^{ns} ±1.45	461.25^{ns} ±102.07
Corriandrum-pre-4h	338.68* ±37.12	339.47* ±38.77	53.43* ±7.60	759.08* ±244.27

Histopathological examination also provided supportive evidence for the results obtained for the enzyme analysis. Microscopically, control livers stained with haematoxylin and eosin showed normal parenchymal architecture with cords of hepatocytes, portal spaces and terminal veins without noticeable alterations.

Morphologically, the liver appeared dark and congested in paracetamol intoxicated mice. Histologically, the liver showed signs of confluent necrosis with valcuolation, infiltrations and ballooning necrosis in the surviving hepatocytes. An improvement in the histopathology was observed in *Corriandrum* treated mice compared to the paracetamol control group. Overall results indicated that pre-treatment is better than post-treatment.

Discussion

Acetaminophen (4-hydroxy acetanilide) was metabolized to the reactive metabolite, NAPQI and once formed, this metabolite conjugates and depletes cellular reduced glutathione level and then binds extensively to the sulfhydryl groups of the cellular proteins. (Tirmenstein & Nelson, 1990) Increase in hepatic GSH level in *Corriandrum* pre-treated mice may result from the enhancement of either *de novo* GSH synthesis or GSH regeneration or both. As a consequence of the action of *Corriandrum* in GSH metabolism, hepatic GSH level can be sufficiently maintained to counteract the increased formation of free radicals as in the case of carbon tetrachloride toxicity. (Ko et al, 1995).

The mechanism by which *Corriandrum* exert its protective action against the hepatotoxin induced alterations in the liver is not clear.

While the present investigation has scientifically confirmed the usefulness of *Corriandrum sativum* as an effective hepatotonic, further studies are needed to elucidate its exact mechanism of action.

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