
Will Herbal-Paracetamol Combination Drug Prevent both Liver and Kidney Disease? - Results and Possibilities

Anjali Sharma, Mukesh Makwana and H.S. Rathore*

Cell Biology Unit, School of Studies in Zoology and Biotechnology
Vikram University, Ujjain 456010. India
*Contact: hrvuz2000@yahoo.co.in

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ABSTRACT

An attempt has been made to briefly review the existing information on herbal compounds which could combat acetaminophen (paracetamol) toxicity. A careful perusal of literature revealed that acetaminophen overdose not only damages liver but also the kidney. Nevertheless, the kidney was badly ignored in studies aimed at preventing paracetamol toxicity with herbal drugs. On account of such major neglect, so far no herbal-paracetamol combination could be made. Milk thistly is only well researched drug which appears as a suitable future candidate, but its action towards the kidney must be studied. The importance of such studies in the future is discussed.

Key words: Acetaminophen/paracetamol, hepatotoxicity, Nephrotoxicity, Herbal Drugs/combination.

INTRODUCTION

Acetaminophen (Paracetamol: N-acetyl-p-aminophen) is an effective analgesic - antipyretic drug which is often used to treat pain and fever. Acetaminophen is available without prescription in many parts of the world (Goodman and Gilman 1996).

The most serious adverse effect of acute overdose of acetaminophen is dose-dependent, potentially fatal hepatic necrosis (Thomas 1993) which may be associated with renal tubular necrosis (Goodman and Gilman 1996). The number of self poisoning suicides with acetaminophen has grown alarming in recent years (Goodman and Gilman 1996; Gyamlani and Parikh 2002). According to a study in USA paracetamol was found to be associated with more than 10, 00, 00 cases of poisoning, 56000 visits to emergency departments, 26000 hospitalization and 450 deaths a year (BMJ 2002). Also acetaminophen was the drug most commonly taken in United Kingdom (Howton et al 1997) causing substantial number of deaths (Bray 1993). Cases of overdoses of acetaminophen in India are also not uncommon (Sharka et al. 1999).

The principal antidotal treatment is the administration of sulphhydryl compound like N-acetyl-cysteine which act by replenishing hepatic stores of glutathione. This drug is effective only if given orally or intravenously within less than 10 hours after ingestion (Smilkstein et al 1988).

BRIEF REVIEW OF EXISTING REPORTS

In the past, several herbal compounds have also been screened to test their ability to reduce and / or nullify acetaminophen induced hepatotoxicity. These reports are given subsequently. It is of interest to mention here that only in two studies both liver and kidney were taken into consideration (Lee et al. 2002 and Bagchi et al. 2002) otherwise the kidney is badly ignored. However, quite earlier it was suggested that special caution should be taken in patients with liver and kidney disease while using paracetamol (Brzeznicka and Piotrowsi 1989).

BRIEF REVIEW OF EXISTING REPORTS
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Worker et al.</th>
<th>Year</th>
<th>Model</th>
<th>Name of the herbal Compound</th>
<th>Hepato protective property</th>
<th>Nephro protective property</th>
<th>Parameters</th>
<th>Lethality test</th>
<th>Histo - pathology</th>
<th>Biochemical / clinical / other parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Akintonwa et al.</td>
<td>1990</td>
<td>Rat</td>
<td>Garcinia Kola</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Glutathione oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT)</td>
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<td>2</td>
<td>Handa et al.</td>
<td>1990</td>
<td>Rat</td>
<td>Andrographis paniculata</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>GOT, GPT, ALP, bilirubin, bilirubin,ALT</td>
</tr>
<tr>
<td>3</td>
<td>Donatus et al.</td>
<td>1990</td>
<td>Hepatocytes</td>
<td>Curcuma longa (Curcumin)</td>
<td>Yes (cytotoxicity)</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Lipid peroxidation, LDL - leakage, GSH - depletion</td>
</tr>
<tr>
<td>4</td>
<td>Ansari et al.</td>
<td>1991</td>
<td>Rat</td>
<td>Picrorhiza kurroa</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Various biochemical parameters</td>
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<tr>
<td>5</td>
<td>Chattopadhyay et al.</td>
<td>1992</td>
<td>Rat</td>
<td>Azadirachta indica</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>GOT, GPT, acid phosphatase, alkaline phosphatase</td>
</tr>
<tr>
<td>6</td>
<td>Mutiel et al.</td>
<td>1992</td>
<td>Rat</td>
<td>Silmarin</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Liver glutathione, lipid peroxidation, glycochen &amp; serum alkaline phosphatase(ALP), gamma-glutamyltransferase, gamma-glutamyltransferase(GGT P) glutamic pyruvic transaminase (GPT)</td>
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<tr>
<td>7</td>
<td>Yamada et al.</td>
<td>1993</td>
<td>Rat</td>
<td>Scizandra fruits (gymnema A)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>(degeneration and necrosis of hepatocytes) Serum amino transferase activity and hepatic liperoxidase content, glutathione</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Gilani et al.</td>
<td>1994</td>
<td>Mice &amp; Rat</td>
<td>Artemisia scoparia</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>GOT, GPT</td>
</tr>
<tr>
<td>9</td>
<td>Cheng et al.</td>
<td>1994</td>
<td>Mice &amp; Rat</td>
<td>Hippophae rhamnoides</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>MDA, GPT, GOT, GSH</td>
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<tr>
<td>10</td>
<td>Lin et al.</td>
<td>1994</td>
<td>Mice</td>
<td>Wedelia chinensis</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>GOT, GPT</td>
</tr>
<tr>
<td>11</td>
<td>Lin et al.</td>
<td>1995</td>
<td>Rat</td>
<td>Sinningia turan folk medicine (Elephantopus scaber L. E.mollis H.B.K. and Pseudoelephantopus spicatus (H.Kroh))</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>GOT, GPT</td>
</tr>
<tr>
<td>12</td>
<td>Singh et al.</td>
<td>1995</td>
<td>Rat</td>
<td>Asimine grasseolens &amp; Hygrophiha auriculata</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Bile duct inflammation, glutathione level, plasma aspartate amino transferase, cell viability, lactate dehydrogenase(LDH)</td>
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<tr>
<td>13</td>
<td>Thabrew et al.</td>
<td>1995</td>
<td>Mice &amp; cultured Rat Hepatocytes</td>
<td>Ophicea octandra</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Alcoholic phosphatase (ALP), GOT, GPT</td>
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<tr>
<td>14</td>
<td>Junba et al.</td>
<td>1995</td>
<td>Mice &amp; Rat</td>
<td>Artemisia maritima</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>GOT, GPT</td>
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<tr>
<td>15</td>
<td>Gilani et al.</td>
<td>1995</td>
<td>Mice &amp; Rat</td>
<td>Cyperus scariosus</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<td>16</td>
<td>Rasheed et al.</td>
<td>1995</td>
<td>Mice</td>
<td>Teucrium stockianum</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Aspartate amino transferase, bilirubin, GSH, liver weight, pento barbitone induced sleeping time.</td>
</tr>
<tr>
<td>17</td>
<td>Chin et al.</td>
<td>1996</td>
<td>Rat</td>
<td>Ham-hong-Chiao Taiwan folk medicine (Bilens pilosa 1...var minor (Blume)Sheriff, B. Pilosa L. and B. Chilensis DC)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>GOT, GPT</td>
</tr>
<tr>
<td>18</td>
<td>Gilani et al.</td>
<td>1996</td>
<td>Mice &amp; Rat</td>
<td>Fumaria parviflora</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>ALP, GOT, GPT</td>
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<td>19</td>
<td>Wang et al.</td>
<td>1996</td>
<td>Mice</td>
<td>Garlic</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>ALT, LDH &amp; GSH</td>
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<tr>
<td>20</td>
<td>Lin et al.</td>
<td>1997</td>
<td>Rat</td>
<td>Scutellaria jurtetrix (Han- dho-Iain)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>GOT, GPT</td>
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<tr>
<td>21</td>
<td>Subramaniam et al.</td>
<td>1998</td>
<td>Rat</td>
<td>Trichopus zylinicus</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Serum marker enzymes, level of lipid peroxidase in liver</td>
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<tr>
<td>22</td>
<td>Ryu et al.</td>
<td>1998</td>
<td>Rat</td>
<td>Artemisia asiatica (DA- 9601)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>(centrilobular necrosis, vacuolar degeneration, inflammation cell) ALT, AST, LDH, GSH</td>
<td></td>
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<tr>
<td>23</td>
<td>Rusu et al.</td>
<td>1999</td>
<td>Rat</td>
<td>Corylus avellana</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>GOT, GPT, SDH, GSH, G-6 Pase and APase, steatosis by sudan black staining</td>
</tr>
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<td>24</td>
<td>Jaff et al.</td>
<td>1999</td>
<td>Rat</td>
<td>Cassia occidentalis</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>AS, ALT, ALP, cholesterol, Total lipid</td>
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<tr>
<td>25</td>
<td>Kuran et al.</td>
<td>1999</td>
<td>Rat</td>
<td>Swertia chirica</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>-</td>
<td>-</td>
<td></td>
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<tr>
<td>26</td>
<td>Lin et al.</td>
<td>2000</td>
<td>Rat</td>
<td>Acathopanax senticosus</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>AST, ALP</td>
</tr>
<tr>
<td>27</td>
<td>Junba et al.</td>
<td>2000</td>
<td>Rat</td>
<td>Berberis aristata (Berberine)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>ALP, AST, ALT</td>
</tr>
<tr>
<td>28</td>
<td>Lin et al.</td>
<td>2000</td>
<td>Rat</td>
<td>Annonaceae fomusamus Family (Gymnosperm peniophyllum)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>(necrosis in the centrilobular area, sinusoidal congestion, infiltration of the lymphocytes and kuffer cells around the hepatic central vein, loss of cell boundaries and ballooning degeneration) AST, ALT</td>
</tr>
<tr>
<td>29</td>
<td>Mandal et al.</td>
<td>2000</td>
<td>Rat</td>
<td>Ficus hofalda</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>GOT, GPT, bilirubin, ALP</td>
</tr>
<tr>
<td>30</td>
<td>Ray et al.</td>
<td>2000</td>
<td>Mice</td>
<td>BH 636 Grape seed proanthoxxys- inidene extract</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>(apoptosis + necrosis, DNA fragmentation) ALT, BUN, CPK</td>
<td></td>
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<tr>
<td>31</td>
<td>Yang et al.</td>
<td>2000</td>
<td>Mice</td>
<td>Yang-Gun-Wan</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>(necrosis) ALT, SDH</td>
<td></td>
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<tr>
<td>32</td>
<td>Emmanuel et al.</td>
<td>2001</td>
<td>Rat</td>
<td>Wedelia calendulae (Coumestans)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>LDH, ALT, ALP, ALT</td>
</tr>
<tr>
<td>33</td>
<td>Wang et al.</td>
<td>2001</td>
<td>Mice</td>
<td>Astragalus (total flavonoids)</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>(hepato cellular necrosis) ALT paraacetamol prolonged pentobarbitol induced sleeping time, paraacetamol and its metabolites in mice urine</td>
<td></td>
</tr>
<tr>
<td>34</td>
<td>Ali et al.</td>
<td>2001</td>
<td>Mice</td>
<td>Rhiayu stricta</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Pentobarbitone induced sleeping time, GSH, AST, ALT, gamma glutamyl transferase (GOT), cholestrol, liver weight</td>
</tr>
</tbody>
</table>
35 Datta et al. 2001 Mice herbal protein C1 (from Cajanus indicus) Yes No No No GPT, GPT, bilirubin, ALP
36 Bhakta et al. 2001 Rat Cassia fistula Yes No No No GPT, GPT, bilirubin, ALP
37 Wu et al. 2001 Rat Legumes (Mung bean, adzuki bean, black bean and rice bean) Yes No No No GPT, GPT
38 Ahmed et al. 2001 Rat Ambrosia maritima Yes No No No AST, ALP, malondialdehyde (MDA), glutathione (GSH), glutathione reductase (GSR-H), glutathione peroxidase (GSH-Px), glutathione - S-transferase (GST)
39 Reen et al. 2001 Cultured Rat Hepatocytes Swerita species Yes No No No GSH, leakage of LDH as biological end-point of toxicity
40 Ye et al. 2001 Mice and Rat Angelica sinensis Yes No No No ALT, hepatic nitric oxide synthase (NOS) activities, GSH, MDA
41 Lin et al. 2001 Rat Vernonia cinerea (Panicalgin and Panicalin) Yes No No No AST, ALT
42 Hittori et al. 2001 Mice Apoene (a garlic derived sulfur-containing compound) Yes No No No GSH, GPT, hepatic protein thiol content
43 Echard et al. 2001 Rat Combination of medicinal herbs Yes No No No AST, ALT
44 Lee et al. 2002 Rat Chinese yam Yes Yes No Yes (renal tubular degeneration changes, necrosis, disintegration, inflammation of central vein and necrosis of liver tissue)
45 Bagchi et al. 2002 Mice Grape seed proanthocyanidine extract Yes Yes No Yes (apoptosis + necrosis + DNA damage) Serum chemistry
46 Ko et al. 2002 Rat Silene aprica Yes No No No Morphological and biochemical observations.
47 Jaudae et al. 2002 Mice & Rat Menthol Yes No No Yes No ALP, AST, ALT
48 Jaudae et al. 2002 Mice & Rat Rutin Yes No Yes No AST, ALT
49 Bhattacharya et al. 2003 Rat Himolive (a polyherbal formulation) Yes No No No GPT, GPT, ALP, thiobarbituric acid-reacting substances (TBARS) SOD, CAT, catalase; phospholipid hydroperoxide, hydroperoxidase; phospholipid-ethanolamine hydroperoxidase
50 Gamal el-din et al. 2003 Mice Arabic gum Yes No No No AST, ALP, lip peroxidation, nitrate + nitrates
51 Kumar et al. 2004 Rat Triautema portulacastrum Yes No No No GPT, GPT, ALP, bilirubin, total Protein
52 Devi et al. 2004 Rat Premna tomentosa Yes No No No Cholesterol, triglycerides, free fatty acids, phospholipids, serum lipoproteins, lipid metabolizing enzymes.
53 Tabassum et al. 2004 Mice Eclipta alba Haevik Yes No No Yes (centrilobular and focal necrosis, ballooning in liver) ALT
54 Shon et al. 2004 Mice Moutan Cortex Yes No No No DNA fragmentation ALT, GSH, Cyt P450 2E1-dependent aniline and p-nitrophenol hydroxylases activities
55 Han et al. 2004 Rat Adzuki bean hulls Yes No No No GSH, GSH-S, GSH-Px, AST, catalase, phospholipid hydroperoxide, phospholipid-ethanolamine hydroperoxidase
56 Rao et al. 2004 Rat Ulva reticulata Yes No No No Aspartate transaminase, alanine transaminase, lipid peroxides, superoxide dismutase, catalase, glutathione, Vit E and C.
57 Gupta et al. 2004 Rat Bauhinia racemosa Yes No No No GPT, GPT, ALP, SOD, CAT, LPO, GSH, bilirubin, total Protein
58 Kim et al. 2004 Rat & cultured rat hepatocytes Alnus japonica Yes No No No Lipid peroxidation, superoxide dismutase, Catalase
59 Mouch et al. 2004 Rat Centaurium erythraea Yes No No Yes GPT, GPT, LDH
60 Porchiaz et al. 2005 Rat Abutilon indicum Yes No No No Enzymatic examination GPT, GPT, ALP, bilirubin, total protein, lipid peroxidation GSH, SOD, catalase activity
61 Munghesh et al. 2005 Rat Berberis tinctoria Yes No No No GPT, GPT, ALP, bilirubin, catalase, iron & total protein concentrations, lipid peroxidation products (thiobarbituric acid (TBARS) reactive substances (TBARS)
62 Oliveira et al. 2005 Mice Pustum heptaphyllin (alpha- and beta- amylin) Yes No Yes Yes (centrilobular necrosis, cell infiltration) ALT, AST, GSH, pentobarbital sleeping time
63 Raghavendran et al. 2005 Rat Sargassum polycystum (Brown algae) Yes No No No Lipid peroxidation, SOD, CAT, GSH, GPx, GST
64 Yi et al. 2006 - Bisnvestelia nervosa (Oleo-gum-resin) Yes No No No Serum marker enzymes and liver weight
65 Kim et al. 2006 Rat Glycyrrhiza radix (liquiritigenin) Yes No No Yes (hepatic necrosis, inflammation) ALT, LDH
66 Baheti et al. 2006 Rat Hemidesmus indicus Yes No No No GPT, GPT, ALP, Bilirubin
67 Iwulokan et al. 2006 Mice Vernonia amygdalina Yes No No No GPT, GPT, ALP, bilirubin, catalase, iron & total protein concentrations, lipid peroxidation products (thiobarbituric acid (TBARS) reactive substances (TBARS)
68 Sadaivan et al. 2006 Rat & In vitro Hedystis corymbosa Yes No No Yes SOD, GPT, SAKP, bilirubin, hexobarbital-induced sleeping time, antilipid peroxidant effect in vitro.
69 Shyamal et al. 2006 Rat Fitziporum nechherreum sight & shrn. Yes No No Yes GPT, GPT
70 Pandey et al. 2006 Rabbit Livol, Eclipta alba and Silybum marianum Yes No No Yes (varying degree of congestion, degeneration and necrosis, areas of focal mononuclear cell infiltration enlarged biliary ducts and perportal oedema) ALT, AST, ALP, LDH, MDA, glutamate dehydrogenase.
72 Parial et al. 2006 Rat Carica papaya Yes No No No GOT, GPT, ALP, Total bilirubin, ALT, AST, tumor necrosis factor alpha (TNF-alpha) in blood, GSH, MDA, myeloperoxidase (MPO) activity, collagen content in liver tissues, luminol and lucigenin CL levels.

73 Sener et al. 2006 Mice Ginkgo biloba Yes No No Yes ALT, AST, ALP, total bilirubin, liver weight.

74 Roy et al. 2006 - Psidium guajava Yes No No Yes AST, ALT, ALP, collagen content in liver tissue, luminol and lucigenin CL levels.

75 Yen et al. 2007 Rat Cuscuta chinensis Yes No No No GPT, GOT, ALP, SOD, catalase, glutathione peroxidase (GPX), malondialdehyde (MDA).

76 Lin et al. 2007 Rat Chai-Hu-Ching-Kan-Tang Yes No No Yes (central necrosis, fatty changes) GOT, GPT, lipid peroxides, SOD, GPX.

77 Setty et al. 2007 Rat Calotropis procera Yes No No No GPT, GOT, ALP, total bilirubin, cholesterol, HDL, tissue GSH.

78 Chaturvedi et al. 2007 Rat Raphanus sativus Yes No No No Thiobarbituric acid reactive substances (TBARS), GOT, GPT, GSH, catalase.

79 BR et al 2008 Rat Phyllanthus polyphyllus Yes No No Yes AST, ALT, ALP, total bilirubin, gamma glutamate transpeptidase (GGPT), lipid peroxides (LPO), total protein, SOD, catalase, GPX, glutathione S-transferase (GST).

DISCUSSION

Only for brevity and convenience current status of knowledge on herbal drugs versus paracetamol poisoning is discussed under following separate headings:

1. Many factors enhance paracetamol toxicity:
   Alcohol, many drugs rifampicin, phenobarbital, isoniazid, phenytoin and carbamazepin increase paracetamol toxicity (Whitecomb and Block, 1994; Willacy, 2007). Even fasting greatly increases the chances of liver damage by paracetamol (Whitecomb and Block, 1994). Tobacco is found as an independent risk factor in paracetamol poisoning (Schmidt and Dalhoff, 2003).

2. Some herbal drugs can reduce paracetamol toxicity
   Chinese medicine Artemisia asiatica. & A. Maritima (DA-9601) has been reported to reduce liver damage induced by paracetamol (Ryu et al., 1998, Janbaz and Gilani, 1995). Another chinese herbal medicine ‘gomsin-A’, a lignan component of Schisandra chinesis has also been reported to be hepatoprotective against paracetamol. It must be noted that inadequate clinical research with human subjects has been conducted on these herbal drugs to confirm the value of these herbal therapies against the toxic side effects of paracetamol (IBIS medical com., 2000). A literature review on herb-drug interaction also mentions that reported herb-drug interactions were based on case reports and were of limited clinical observations (Hu et al., 2005). On account of such badly ignored limited clinical observations on herb-drug interaction so far no herbal paracetamol combination drug could be made. On the contrary recently nitroparacetamol (NCX-701) has been introduced as a novel analgesic drug (Sandoval et al., 2007). Silybum marianum (milk thistle) reduces paracetamol induced hepatotoxicity in animals. This is a well research herbal drug in animals and humans and has good future (Pradhan and Girish, 2006) but its preventive action towards kidney needs detail studies.

3. Problem in developing country like India:
   In developing country like India where self medication with herbal and other drugs without prescription is a common practice hence chances of accidental or intentional overdose always exists. Moreover general public is not aware of drug abuse and its antidotal management under such circumstances paracetamol induced liver and kidney damage may go unnoticed and affected individual may die. Citizen and villagers know use paracetamol but none of them know about its hepatonephrotoxicity and about its principal antidotal drug N-acetylcysteine. Liver transplantation is also out of reach of general public. This drug is effective only when administrated within 10 hours of paracetamol poisoning and this drug is not available every where in India.

CONCLUSION
It is needless to say that paracetamol induced hepatonephrotoxicity and its management with herbal drugs also deserves serious attention, no matter, renal insufficiency occurs in about 1-2 percent cases of paracetamol overdose.

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