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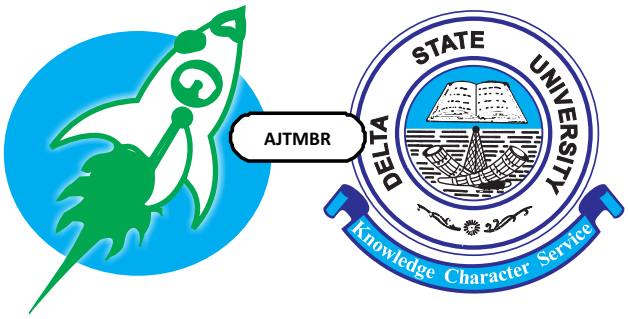

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Focus and Scope

The African Journal of Tropical Medicine and Biomedical Research is a multidisciplinary and international journal published by the College of Health Sciences, Delta State University of Abraka, Nigeria. It provides a forum for Authors working in Africa to share their research findings on all aspects of Tropical Medicine and Biomedical Sciences and to disseminate innovative, relevant and useful information on tropical medicine and biomedical sciences throughout the continent. The journal will publish original research articles, reviews, editorials, commentaries, short reports, case reports and letters to the editor. Articles are welcome in all branches of medicine and dentistry including basic sciences (Anatomy, Biochemistry, Physiology, Pharmacology, Psychology, Nursing etc) and clinical sciences (Internal Medicine, Surgery, Obstetrics and Gynaecology, Dental surgery, Child Health, Laboratory Sciences, Radiology, Community Medicine, etc). Articles are also welcome from social science researchers that document the intermediating and background social factors influencing health in countries of Africa. Priority will be given to publication of articles that describe the application of the principles of primary health care in the prevention and treatment of diseases.

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Table of Contents

Fruit Peels of Citrus Tangerina Attenuate the Oxidative Stress and Cell Damage Caused by Acetaminophen on Wistar Rats

Moke EG[1], Umukoro EK[1], Anachuna KK[2], Duabry TME[2], Ezedom T[3], Asiwe JN[4]

ABSTRACT

Introduction: The regulation of the physiological processes in the body is one of the vital roles of the liver. Hepatic damage or liver dysfunction is a major health concern in the society. The need to explore alternative drugs for the treatment of hepatic diseases necessitated the present study on the effect of fruit peels extract of *Citrus tangerina* on acetaminophen-induced hepatotoxicity in Wistar rats.
Materials and methods: Animals were grouped as follows: group I received normal diet, group II was given acetaminophen 500 mg/kg/day, groups III and IV received fruit peel extracts of *Citrus tangerina* at 200 and 400 mg/kg/day respectively, while group V received silymarin 100 mg/kg/day (standard drug). Groups III-V were simultaneously administered acetaminophen 500 mg/kg/day to induce hepatotoxicity. All drugs were given orally. At the end of a 7-days experimental period, the animals' serum and liver were obtained for biochemical and histopathological analyses.
Results: Results of this study showed that acetaminophen dosing increased serum AST (aspartate transaminase), ALT (alanine transaminase) and ALP (alkaline phosphatase), as well as decreased antioxidant enzymes. Treatment with *C. tangerina* fruit peel extract significantly reversed acetaminophen hepatotoxic effect in a dose-dependent manner.
Conclusion: This study suggests that *C. tangerina* fruit peel extract possesses antioxidant property and attenuates liver damage induced by acetaminophen in Wistar rats.
Keywords: acetaminophen, *Citrus tangerina*, flavonoid, antioxidants

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Introduction

The regulation of the physiological processes in the body is one of the vital roles of the liver. The liver is involved in the metabolism clearance of most chemicals, including drugs, and toxins.The metabolic functions of the liver are important for the removal of waste, the accumulation of which causes complications to the body[1].Hepatic damage or liver dysfunction is a major health concern in the society. Chronic exposure of the liver to certain chemical substances, alcohol, long-term drug therapy, and even commonly prescribed medicines such as acetaminophen and diclofenac, affect hepatic functioning. Some disease conditions have been implicated in liver dysfunction. Overdose of acetaminophen(paracetamol)

can cause acute liver failure and even death[2,3]. Hepatotoxic effect of acetaminophen has been shown to be due to its toxic metabolite, N-acetyl-p-benzoquinineamine which binds to macromolecules of the liver cells resulting in cell necrosis[4].

Treatment of common liver diseases with various synthetic antioxidants like butylated hydroxyanisole and butylatedhydroxytoluene and also conventional drugs like corticosteroids, antiviral and immunosuppressants are quite unsafe and accompanied with serious adverse effects[5]. Hence, the need to explore alternative drugs with lesser side effects for the treatment of hepatic diseases. Herbal medicine involving the use of natural remedies from medicinal plants for medical therapy is now on the rise, particularly in developing regions like Africa, as it is considered to be efficient and safe[6]. Majority of these medicinal plants have been shown to possess pharmacological activities[7-15].

Citrus tangerina (family, Rutaceae) has been used as folk medicine across the African, Asian, and South American continents. Parts of the plant possess biological properties which have been shown to be medicinal[16,17]. Free radical scavenging activity and oxidative stability of *C. tangerina* oils extracted from the seeds of citrus have been reported[18,19]. Little or no research to the best of our knowledge, have been carried out to evaluate the effect of fruit peels extract of *C. tangerina* on antioxidant status of acetaminophen-induced hepatotoxicity in Wistar rats, thus, the aim of this present study.

Materials and Methods

Plant material and preparation of extract

Citrus tangerina fruits were collected from the local market of Abraka, Nigeria and authenticated in the Department of Botany, Faculty of Sciences, Delta State University, Abrakaby a taxonomist (Dr. A.H.Erhenhi). The fruits' peels were rinsed properly with water, air-dried, and powdered. The powdered peel of *Citrus tangerina* (1.67 kg) was extracted exhaustively with 3200 ml of 70% methanol using Soxhlet evaporator at 25-35^{0}C. The filtrate was further concentrated to dryness with the aid of a water bath set at 40 ^{0}C. The weight of the final extract was recorded and stored in the refrigerator prior to the study.

Animals

Wistar rats (150 – 200 g) were procured from Animal House, Faculty of Basic Medical Science, Delta State University, Abraka, Nigeria. The animals were acclimatized for a period of two weeks under standard conditions before starting the study, and were fed rat feed and portable water *ad libitum*. Guidelines followed in the handling of animals were in accordance with the global standard adopted by the Ethical Committee of the Faculty of Basic Medical Science, Delta State University, Abraka, Nigeria.

Experimental design

The rats were randomly placed into five groups, n = 5:

Group I – Normal Control, rats were fed with normal diet for 7 days.

Group II – Acetaminophen Control, rats were given acetaminophen at 500 mg/kg daily for 7 days.

Group III–*C. tangerina* 200, rats were simultaneously given acetaminophen at 500 mg/kg daily + *Citrus tangerina* peel extract at 200 mg/kg daily for 7 days.

Group IV - *C. tangerina* 400, rats were simultaneously given acetaminophen at 500 mg/kg daily + *Citrus tangerina* peel extract at 400 mg/kg daily for 7 days.

Group V– Silymarin (standard drug

treatment), rats were simultaneously given acetaminophen at 500 mg/kg daily + silymarin at 100 mg/kg daily for 7 days.
The experimental animals were orally administered the extracts or silymarin once daily for 7 days. All the animals except the normal control group were administered acetaminophen 500mg/kg/day orally for 7 days[20] before blood samples were collected under chloroform anaesthesia by cardiac thoracic puncture into plain sample bottles and centrifuged at 4000 rpm for 10 min. The serum obtained was used to estimate biochemical paraments. Antioxidants activity via the estimation of serum level of superoxide dismutase (SOD), catalase (CAT) and malondialdehyde (MDA)was analyzed[21-23]. Methods of Reitman and Frankel[24] and Roy[25] were used in determining **a**lkaline phosphatase (ALP), aspartate aminotransefrase (AST), and alanine transaminase (ALT) in serum.

Histopathological studies
The liver was harvested for histopathological studies using haematoxylin-eosin staining method. The tissues were processed andembedded in paraffin wax. Sections of liver tissue were cut and stained with hematoxylinand eosin following standard microtechnique, and were examined under the microscope to analyze the histopathological changes in the liver, with micrographs taken.

Data analysis
Results are presented as the mean ± standard error of the mean (SEM). Data were analyzed using one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. P-values < 0.05 were taken as significant. Data were processed by GraphPad Prism software version 7.

Results

Biochemical assay
There was significant ($P<0.05$) increase in the serum liver enzymes (AST, ALT, and ALP) of rats in the acetaminophen (ACM) control group as compared with those in the normal control group. Administration of 200 mg/kg and 400 mg/kg of *C. tangerina* peel extracts resulted in significant ($P<0.05$) reduction in serum AST. At 400 mg/kg, the extract also significantly ($P<0.05$) reduced serum ALT and ALP levels when compared to the acetaminophen control group. Significant ($P<0.05$) decrease in AST was observed in silymarin-treated rats when compared to the acetaminophen control group. (Table 1)

Non-significant ($P>0.05$) increase in kidney function indices (urea and creatinine) was seen with the acetaminophen control group when compared with the normal control group. Both doses of *C. tangerina* (200 and 400 mg/kg) showed significant ($P<0.05$) decrease on serum urea and creatinine when compared to the acetaminophen control group. Similarly, silymarin significantly ($P<0.05$) decreased urea and creatinine (Table 1).

Comparative significant ($P<0.05$) decrease in serum antioxidant levels (SOD and CAT) and increase in MDA (lipid peroxidation biomarker) were observed in acetaminophen control group as against those in the normal control group. A significant ($P<0.05$) increase in SOD and CAT enzymes with decreased MDA were seen in rats administered *C. tangerina* peel extract at doses of 200 and 400 mg/kg as compared with the acetaminophen control group. (Table 2)

Histopathological analysis
Histopathological analysis of the liver tissues showed massive necrosis of hepatocytes and hepatic congestion, with extensive infiltration by macrophages obviously induced by

acetaminophen administration. Simultaneous treatment with *C. tangerina* peel extracts or silymarin diminished the level of hepatic lesions induced by the hepatotoxin. The observed alterations of the liver architecture coincided with the corresponding changes in the enzyme levels, thus the hepatoprotective effect of *C. tangerina* fruit peel extract was established. (Figure 1)

Table 1: Effect of *Citrus tangerina* fruit peel on liver and kidney parameters in acetaminophen (PCM)-induced hepatoxicity in rats

	AST (IU/L)	**ALT (IU/L)**	**ALP (IU/L)**	**Urea (mg/dL)**	**Creatinine (mg/dL)**
Normal Control	46.41 ± 1.51	11.53 ± 1.79	31.23 ± 3.27	16.30 ± 0.64	2.63 ± 0.05
ACM control	66.71 ± 0.94 *	18.92 ± 3.18 *	48.77 ± 1.18 *	19.43 ± 2.78	3.80 ± 0.34
C. tangerina 200	48.74 ± 0.71 **	13.66 ± 2.13	38.70 ± 3.18	14.76 ± 0.61 **	2.81 ± 0.51 **
C. tangerina 400	48.55 ± 1.17 **	9.64 ± 1.76 **	35.70 ± 2.20 **	10.10 ± 0.80 **	2.25 ± 0.35 **
Silymarin	48.86 ± 0.75 **	13.94 ± 1.85	40.42 ± 2.04	7.26 ± 0.54 **	2.23 ± 0.76 **

All values are expressed as mean ± standard error of mean (SEM); n=5
** = P<0.05 when compared with normal control;** = P<0.05 when compared with acetaminophen control group*

Table 2: Effect of *Citrus tangerina* fruit peel on antioxidative parameters in acetaminophen (PCM)-induced hepatoxicity in rats

	SOD (IU/L)	**CAT(IU/L)**	**MDA(IU/L)**
Normal Control	0.59 ± 0.03	1.02 ± 0.05	0.41 ± 0.06
ACM control	0.37 ± 0.04 *	0.55 ± 0.09 *	0.73 ± 0.07 *
C. tangerina 200	0.65 ± 0.01 **	0.93 ± 0.01 **	0.42 ± 0.04 **
C. tangerina 400	0.77 ± 0.01 **	1.12 ± 0.06 **	0.40 ± 0.02 **
Silymarin	0.99 ± 0.05 **	1.51 ± 0.04 **	0.42 ± 0.04 **

All values are expressed as mean ± standard error of mean (SEM); n=5
** = P<0.05 when compared with normal control;** = P<0.05 when compared with acetaminophen control group*

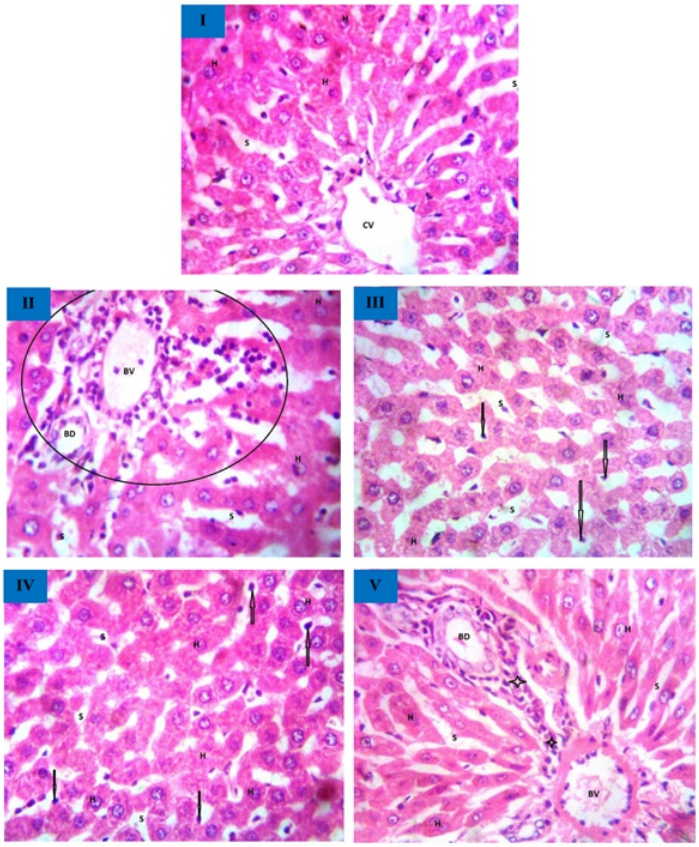

Figure 1: Photomicrograph of liver histology. **I** (normal control) – shows hepatic tissue free from inflammatory cells and congestion; **II** (acetaminophen control) – shows marked periportal hepatitis (circle) infiltrated by inflammatory cells; **III** (*C. tangerina* 200) – shows moderate activation of hepatic macrophage (arrow) within the sinusoids; **IV** (*C. tangerina* 400) – shows mild hepatic macrophage (arrow) within the sinusoids; **V** (silymarin) – shows mild periportal inflammatory cells infiltration (star) with sinusoids free from congestion. *(CV–central vein; H–hepatocytes; s–sinusoids; BV–blood vessel; BD–bile duct) (H&E staining; ×400 magnification).*

Discussion

In recent times, search for newer drug of herbal origin is on the rise as researches continue to attempt discoveries at best therapy for hepatic diseases[26]. The present study evaluated the efficacy of methanol fruit peel extract of *C. tangerina* in preventing hepatic cell damage produced by excessive dose of acetaminophen. Acetaminophen elicits its hepatotoxic effect by its toxic phase I metabolite (N-acetyl-p-benzoquinineamine) binding to cellular components of hepatocytes, consequently leading to cell necrosis[4,27]. Silymarin is a well established drug treatment for liver damage[28]. As an antioxidant compound, silymarin scavenges free radicals that are destructive to cell, increases the level of antioxidant enzymes in the liver, and promotes hepatic cell regeneration by stimulating protein synthesis in the liver[29,30].

Acetaminophen resulted in an increase in the levels of serum AST, ALT, and ALP, which are biomarkers of hepatic cell damage and loss of functional integrity[31]. Results from this study revealed that *C. tangerina* fruit peel extract reduced the acetaminophen-induced elevated serum liver function enzymes,

although this effect was profound at the higher dose of 400 mg/kg. This implies that 400 mg/kg of *C. tangerina* fruit peel will improve health status of hepatocytes. Liver histology revealed that *C. tangerina* fruit peel extract can possiblyattenuate hepatic damage induced by acetaminophen. The observed cellular repair by *C. tangerina* fruit peel extract is much similar to that produced by silymarin in this study.

Daily dosing with acetaminophen 500 mg/kg caused a decrease in the serum levels of superoxide dismutase and catalase, and induced lipid peroxidation by increasing malondialdehyde serum level. This resulted in elevation of oxidative stress on hepatic cell[32]. *Citus tangerina* fruit peel extract co-administration with acetaminophen markedly alleviated the induced oxidative stress in a dose-dependent manner by decreasing the elevated MDA level while increasing SOD and CAT levels. This is an indication that generated reactive oxygen species could be scavenged by the fruit peel extract of *C. tangerina*, hence, its oxidative stability potential. The antioxidant effect of *C. tangerina* fruit peel extract may be implicated in the cell damage repair of liver cells as reported in this study (Figure 1).

The hepatoprotective and antioxidant effects of the fruit peel extract of *C. tangerina* may be attributed to the fact that it is enriched with flavonoids and phenolic compounds which have potent antioxidant actions[17,18]. Absorption and neutralization of free radicals, inhibition of enzymes associated with reactive oxygen species (ROS) pathways, and improvement of antioxidant enzymes activities (SOD, CAT, GSH) are basic mechanisms by which these phytochemicals exhibit antioxidant actions[33-36].

Conclusion

The result of this study evidently reveals that alterations produced by the administration of acetaminophen in the various biochemical parameters, namely AST, ALT, ALP, urea, creatinine, SOD, CAT, and MDA were reversed significantly by the treatment with extracts of *C.tangerina* fruit peels. Histopathological examinations of the rat liver supported this finding as shown from the regeneration of hepatocytes upon treatment with *C. tangerina* fruit peel extract. This study suggests that *C. tangerina* fruit peel extract possess antioxidant property and attenuates cell damage in acetaminophen-induced hepatotoxicity.

References

1. Kumar G, Banu GS, Pappa PV, Sundararajan M, Pandian MR. Hepatoprotective activity of *Trianthemaportulacastrum* L. against paracetamol and thioacetamide intoxication in albino rats. J Ethnopharmacol 2004; 92(1):37-40
2. Hodgman MJ, Garrard AR. A review of acetaminophen poisoning. Crit Care Clin 2012;28(4):499-516.
3. Ramachandran A, Jaeschke H. Acetaminophen toxicity: Novel insights into mechanisms and future perspectives. Gene Expr 2018;18 (1):19-30.
4. Chun LJ, Tong MJ, Busuttil RW, Hiatt JR. Acetaminophen hepatotoxicity and acute liver failure. J Clin Gastroenterol 2009;43: 342–349.
5. Zhao Z, Wei Q, Hua W, Liu Y, Liu X. Zhu Y. Hepatoprotective effects of berberine on acetaminophen-induced hepatotoxicity in mice. Biomed Pharmacother 2018; 103: 1319-26.
6. Ekor M. The growing use of herbal

medicines: issues relating toadverse reactions and challenges in monitoring safety. Front Pharmacol 2014; 4: 177.
7. Umeh VN, Ilodigwe EE, Ajaghaku DL, Erhirhie EO, Moke EG, Akah PA. Wound-healing Activity of the Aqueous Leaf Extract and Fractions of *Ficus exasperate* (Moraceae) and its Safety Evaluation on Albino Rats. J Tradit Complement Med 2014; 4(4): 246-252
8. Emudainohwo JOT, Erhirhie EO, Moke EG, Edje KE. A Comprehensive Review on Ethno-Medicine, Phytochemistry and Ethnopharmacology of *Chrysophyllum albidum*. JAdv Med Pharm Sci 2015; 3(4):147-154
9. Ojezele MO, Moke EG, Onyesom I. Impact of generic antimalarial or *Phyllanthus amarus* and vitamin co-administration on antioxidant status of experimental mice infested with *Plasmodium berghei*. Beni-Suef Univ J Basic Appl Sci 2017; 6: 260-265
10. Anachuna KK, Oyem CJ, Nwogueze BC, Asiwe JN. Glucose lowering effects and histomorphological changes of Vernonia amygdalinaon pancreatic compromised wistar rats using alloxan monohydrate. Trop J Health Sci 2018; 25(2): 27-31
11. Issa MT, Agbon AN, Balogun SU, Mahdi O, Bobbo KA, Ayegbusi FO. Hepatoprotective effect of methanol fruit pulp extract of *Musa* paradisiaca on carbon tetrachloride-induced liver toxicity in Wistar rats. J Exp Clin Anat 2018; 17:1-7
12. Ben-Azu B, Aderibigbe AO, Omogbiya IA, Ajayi AM, Iwalewa EO. Morin Pretreatment Attenuates Schizophrenia-Like Behaviors in Experimental Animal Models. Drug Res (Stuttg) 2018; 68(03): 159-167.
13. Moke EG, Oghoghovwe I, Ahante E. The Effect of Omega® Roots + Ginseng Aloe Vera, a Nigerian Herbal Mixture, on Haematological Parameters of Normal Experimental Rats. J Drug DelivTher 2018; 8(3): 29-31
14. Erhirhie EO, Emeghebo CN, Ilodigwe EE, Ajaghaku DL, Umeokoli BO, Eze PM, Ngwoke KG, Chiedu Okoye FBG. *Dryopterisfilix-mas* (L.) Schott ethanolic leaf extract and fractions exhibited profound anti-inflammatory activity. Avicenna J Phytomed2019; 9(4): 396-409.
15. Ruiz-Reyes SG, Villarreal-La Torre VE, Silva-Correa CR, Sagástegui-Guarniz WA, Cruzado-Razco JL, Gamarra-Sánchez CD, *et al*. Hepatoprotective Activity of *Cordia lutea*Lam Flower Extracts Against Paracetamol-Induced Hepatotoxicity in Rats. Pharmacog J 2021;13(2): 309-316.
16. Aruoma OI,Landes B,Ramful-Baboolall D, Bourdon E,Neergheen-Bhujun V, Wagner K,Bahorun T. Functional benefits of citrus fruits in the management of diabetes. Prev Med 2012; 54: S12–S16.
17. Lv X, Zhao S, Ning Z, Zeng H, Shu Y, Tao O, Xiao C, Lu C, Liu Y. Citrus fruits as a treasure trove of active natural metabolites that potentially provide benefits for human health. Chem Cent J 2015; 9: 68.
18. Malacrida CR, Kimura M, Jorge N. Phytochemicals and antioxidant activity of Citrus seed oils. Food Sci. Techmol. Res 2012; 18(3): 399-404.
19. Oikeh EI, Omoregie ES, Oviasogie FE, Oriakhi K. Phytochemical,

antimicrobial and antioxidant activities of different Citrus juice concentrates. Food Sci Nutr2016; 4(1): 103-109.
20. Das A, Borthakur Mk. Hepatoprotective Activity of *Chenopodium Album* Linn. Against Paracetamol Induced Liver Damage in Albino Rats. IJPSR 2020; 11(11): 5605-5610
21. Misra HP, Fridovich I.The role of superoxide in the autoxidation of Epinephrine and simple assay for superoxide dismutase. J Biol Chem 1972; 27: 3170.
22. Sinha AK. Colorimetric assay of catalase. Anal Biochem1972; 47: 389-394.
23. Gutteridge JM, Wilkins S. Copper dependent hydroxyl radical damage to ascorbic acid: formation of thiobarbituric acid reactive product. FEBS Letts 1982; 137: 327-330.
24. Reitman S, Frankel S. A Colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. Am J Clin Pathol1957; 28: 56-63.
25. Roy AV. Rapid method for determining alkaline phosphatase activity in serum with thymolphthalein monophosphate. Clin Chem 1970; 21: 5.
26. Adetutu A,Owoade A. Hepatoprotective and antioxidant effects of Hibiscus polyphenol rich extract (HPE) against carbon tetrachloride (CCl_4)-induced damage in rats. BJMMR 2013; 3(4): 1574-86.
27. Mitchell JR, Jollow DJ, Potter WZ, Gillette JR, Brodie BB. Acetaminophen-induced hepatic necrosis. IV. Protective role of glutathione. J Pharmacol Exp Ther 1973; 187(1): 211-217.
28. Morazzoni P, Bombardelli E. Silybum marianum. Fitoterapia 1995; 66: 3.
29. Fiebrich G, Koch H. Silymarin, an inhibitor of lipoxygenase. Experientia 1979; 35:148-150.
30. Muzes G. Effect of the bioflavonoid silymarin on the in vitro activity and expression of superoxide dismutase (SOD) enzyme. Acta Physiol Hungarica 1991; 78: 3-9.
31. Fu S, Wu D, Jiang W, Li J, Long J, Jia C, Zhou T. Molecular Biomarkers in Drug-Induced Liver Injury: Challenges and Future Perspectives. Front Pharmacol 2020; 10:1667.
32. Cichoż-Lach H, Michalak A. Oxidative stress as a crucial factor in liver diseases. World J Gastroenterol 2014; 20(25):8082-91.
33. Cotelle N. Role of flavonoids in oxidative stress. Curr Top MedChem 2001; 1: 569–590.
34. Mari M, Colell A, Morales A, von Montfort C, Garcia-Ruiz C, Fernandez-Checa JC. Redox control of liver function in health and disease. Antioxid Redox Sign 2010; 12: 1295–1331.
35. Kurutas EB. The importance of antioxidants which play the role in cellular response against oxidative/ nitrosative stress: current state. Nutr J 2016; 15(1):71.
36. He L, He T, Farrar S, Ji L, Liu T, Ma X. Antioxidants Maintain Cellular Redox Homeostasis by Elimination of Reactive Oxygen Species. Cell PhysiolBiochem 2017;44(2):532-553.

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