Review: Hepatoprotector Compounds in Plant Extracts

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ABSTRACT

Many plants have been reported to possess hepatoprotective activity. The mechanism has not yet been revealed, but it was predicted due to the antioxidants that could prevent the formation of free radicals produced by hepatotoxins. Of the 30 plants studied, *Crocus sativus* gave the largest hepatoprotector activity at a dose of 20 mg / kg, followed by *Uncaria gambier* Roxb. with a dose of 30 mg / kg and *Melastoma malabathricum* Leaf at a dose of 50 mg / kg.

Keywords: Liver, CYP450, antioxidant, free radicals

INTRODUCTION

Liver damage can be caused by infection and the activity of chemical compounds that enter the body with various action mechanisms. Liver damage begins with increased steatosis and eventually fibrosis of the liver which can cause death. Although the pathogenesis of fibrosis is unclear, it does not demand that reactive oxygen species (ROS) play a role in pathological changes in the liver, especially in cases of liver disease caused by alcohol and toxins. Cell membrane plays an important role in resisting the effects of ROS so that the process of peroxidation in unsaturated fatty acids on the membrane leads to decreased integrity and membrane function which implies serious pathological changes. Some of the body's natural protective mechanisms are involved in the reduction of liver damage caused by peroxidation. However, due to impaired protection or when increased SOR, additional protective mechanisms through antioxidant consumption are required. Many natural ingredients that exhibit antioxidant properties are advised in the prevention and treatment of liver diseases caused by free radicals (Panjaitan *et al.*, 2011; Maulita *et al.*, 2005).

In Indonesia in 1980- 2010, cirrhosis patients grew and caused mortality, 19.8% (1980), 22.4% (1990), 24.3% (year 2000), 24.8% (year 2010) per 100,000 deaths (Mokdad et al., 2014). From the data obtained by WHO, in 2012 Indonesia was ranked sixth in the world with a percentage of 3.2% as a cirrhosis of the liver causing death. In addition, deaths caused by the disease from 2000 to 2012 continue to increase (WHO, 2015) The use of medicinal plants for health benefits is increasing worldwide. Medicinal plants have a significant contribution to human health that is promotive, curative and rehabilitative, as well as in the prevention of disease (WHO, 2010).

Utilization derived from natural ingredients as a traditional medicine has begun to be developed. The use of natural or herbal ingredients plays a very important role in dealing with the problem of liver damage. Herbs are said to have hepatoprotective effects when its use is able to maintain the function of liver cells and help speed healing. In the last year the focus of research using herbs as hepatoprotective was evaluated through antioxidant mechanisms (Novianto, et al., 2016).

In Indonesia there are many kinds of plants that are believed to have the property as a hebal crop. Therefore, Indonesia has a great opportunity in processing herbs into products that have activity as a hepatoprotektor. Therefore, the expected review of this article can provide scientific information about herbal plants that have activity as a hepatoprotector.

METHOD

The review process of this article was carried out by collecting articles related to the topic from scientific worldwide journals. The articles were then screened and selected. Inclusion criteria are those published during 2013-2018. Other sources are used apart from journal data from WHO website and literature books.

RESULT

The results obtained from journal screening include effective doses of various plants and the activity of compounds that give effect as a hepatoprotector. The hepatoprotector activity test was performed by dividing the test animal into several groups, among which the positive control group, the negative control and the treatment group (the test group) gave effective dose results as a hepatoprotector agent.

Table. 1 Induction, Dosage, and Ingredients of Herbal Plant Compounds that Have Hepatoprotector Activity

No.	Name of Spesies	Compound Content	Induction	Dose Effective mg/kg	References
1	*Allium cepa*	Flavonoid	Ethanol	600	(Eswar Kumar *et al.*, 2013)
2	*Anacardium occidentale*	Flavonoid, Saponin	CCl4	500	(Agbon, Ikyembe and Pwavodi, 2014)
3	*Aquilaria agallocha*	Tannins, Flavonoids, Phenolic	PCT	400	(Alam *et al.*, 2017)
4	*Bauhinia purpurea*	Saponin, Flavonoid, Tanin, Polifenol	PCT	500	(Yahya *et al.*, 2013)
5	*Ceriops decandra* (Griff.)	Flavonoids, Catechin Anthraquinone	CCl4	400	(Gnanadesigan, Ravikumar and Anand, 2017)
6	*Chenopodium bonus-henricus L.*	Flavonoid	CCl4	100	(Kokanova-Nedialkova *et al.*, 2017)
7	*Chonemorpha fragrans*	Flavonoid	PCT, INH	400	(Duraisankar, Devi and Shanmugasundram, 2015)
8	*Citrus hystrix &Citrus maxima*	Flavonoid	PCT	200	(Abirami, Nagarani and Siddhuraju, 2015)
9	*Cosmos caudatus*	Flavonoid, Quersetin	PCT	1125	(Rahman, 2009)
10	*Crocus sativus*	Flavonoid	PCT	20	(Omidi *et al.*, 2014)
11	*Curcuma longa*	Flavonoid	Thioacetamide	250	(Salmah Ismail, 2013)
12	*Dendrophthoe petandra* L	Flavonoid	CCl4	70	(Tristanti, Fatimawali and Bodhi, 2013)
13	*Ecbolium viride* roots	Flavonoids, Alkaloids, Sterols	PCT	400	(Cheedella, Alluri and Ghanta, 2013)
14	*Flacourtia montana*	Flavonoids, Tannins	PCT	200	(Joshy *et al.*, 2016)
15	*Gentiana cruciata* L.	Flavonoid	CCl4	200	(Mihailović *et al.*, 2014)
16	*Gypsophila trichotoma*	Saponarin	CCl4	80	(Simeonova *et al.*, 2014)
17	*Juniperus phoenicea*	Flavonoids, Tannins	CCl4	250	(Laouar *et al.*, 2017)
18	*Liquidambar styraciflua* L. leaves	Flavonoid	CCl4	250	(Eid *et al.*, 2015)
19	*Lophatherum gracile*	Flavonoid, Kumarin	CCl4	800	Thomson, et al., 2016
20	*Lophatherum gracile* Leaves	Flavonoid, Chumarin	CCl4	800	(He *et al.*, 2016)

21	*Macrothelypteris torresiana* (Gaudich.)	Flavonoid, Phenolic Acid	CCl4	300	(Mondal *et al.*, 2017)
22	*Maytenus robusta*	Flavonoid	CCl4	100	(Thiesen *et al.*, 2017)
23	*Melastoma malabathricum* Leaf	Flavonoid, Saponins, And Tannins	PCT, CCl4	50	(Kamisan *et al.*, 2013)
24	*Morinda tinctoria*	Flavonoids And Tannins	PCT	150	(Subramanian *et al.*, 2013)
25	*Nigella sativa*	Flavonoids, Silichristin	PCT	250	(Hamza and Al-Harbi, 2015)
26	*Oldenlandia herbacea*	Flavonoid, Fenol, Saponin, Tanin	D-galactosamine	200	(Pandian, Badami and Shankar, 2013)
27	*Rhodiola imbricata*rhizome	Flavonoids, Coumarins	PCT	400	(Senthilkumar, Chandran and Parimelazhagan, 2014)
28	*Solanum xanthocarpum & Juniperus communis*	Phenolic, Flavonoid	PCT, Azithromycin	400	(Singh *et al.*, 2016)
29	*Tetrapleura tetraptera*	Flavonoid	CCl4	300	(Campanulatus and Tubers, 2009)
30	*Uncaria gambir* Roxb.	Katekin	CCl4	30	(Hasti, Muchtar and Bakhtia, 2012)

DISCUSSION

From the various types of plants studied and known to provide hepatoprotector activity, all these plants contain antioxidants derived from secondary metabolite compounds namely flavonoids. The other secondary metabolite compounds found in some plants such as coumarin, catechins, saponins, phenol compounds and others.

Antioxidants are one of the targets of the hepatoprotective mechanism. Damage to cell membranes and proteins is a sign of oxidative stress caused by free radicals (Panjaitan, et al., 2007). Therefore, antioxidants are needed to convert free radicals into non-reactive compounds.

The usual method of testing hepatoprotector activity can be either in vivo or in vitro. In vivo is done by giving test preparation to the animal by being divided into several groups to see the difference of result from each group to be tested.

From Table 1 it can be seen that *Crocus sativus* gave the largest hepatoprotector activity at a dose of 20 mg / kg, followed by *Uncaria gambier* Roxb. with a dose of 30 mg / kg and *Melastoma malabathricum* Leaf at a dose of 50 mg / kg.

Substances used to induce liver damage are called hepatotoxins, commonly used Paracetamol, Carbon tetrachloride (CCl4), D-Galactosamine, and Thioacetamide. In damaged liver organel damage and cell membranes that can cause ALT and AST enzymes are released into the blood from subel organelles and cytosols. Therefore, the levels of enzymes in the blood vessels will increase (Novianto, 2016)

Based on a review of the source of review data obtained, parameters examined in the test hepatoprotektor, including the biochemical and histopathological parameters. Biochemical parameters include AST, ALT, ALP, total bilirubin, total cholesterol, total glycerides, serum proteins, and antioxidant enzyme activity. As for histopathology by looking at damage to hepatocytes using a microscope.

Increased total bilirubin levels can be caused by a leak of bilirubin from ductuli cells or liver cells that cause bilirubin to enter the bloodstream. Decreased protein levels are caused because liver cells are damaged so that the ability to synthesize proteins decreases. Increased ALP can be caused by the presence of kolestatis, and in extrabiliary obstruction or intrabiliar this enzyme has increased 3-10 times than normal. Increased ALT in the blood is caused by damage to liver cells and skeletal muscle cells. While the AST treatment is caused by severe liver damage accompanied by necrosis (Panjaitan *et al.*, 2011)

CONCLUSION

Many plants have been reported to have hepatoprotector activity with its ability as an antioxidant. This antioxidant compound is one of them is flavonoids. Of the 30 plants studied, *Crocus sativus* gave the largest hepatoprotector activity at a dose of 20 mg / kg, followed by *Uncaria gambier* Roxb. with a dose of 30 mg / kg and *Melastoma malabathricum* Leaf at a dose of 50 mg / kg.

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