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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
ESPS manuscript NO: 13539
Title: Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism
Reviewer code: 02860705
Science editor: Yue-Li Tian
Date sent for review: 2014-08-27 14:18
Date reviewed: 2014-09-09 19:53

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair		BPG Search:	[ ] Rejection
[ ] Grade E: Poor	[ ] Grade D: Rejected	[ ] Existing	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

i read with great interest the review titled "Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism". the review described how the extract of the blueberry leaves counteract the HCV replication and also the host proteins involved in this mechanism. according to my opinion the manuscript is clear and well written even if it will be result also important to understand the way of internalization of this natural compound and if interact with the host receptor used by the virus to entry into the hepatocyte.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
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Title: Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism
Reviewer code: 02860585
Science editor: Yue-Li Tian
Date sent for review: 2014-08-27 14:18
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

In this paper, Ishida et al. review the role of functional foods and ingredients efficient on HCV infection, as well as the chemical structural characteristics of proanthocyanidin and its action mechanism. Althogh new DAAs have dramatically increased the SVR rates in Hepatitis C in Western areas, some cost-sensitive countries have still peginterferon and ribavirin like gold standard therapy. Therefore, the aim is relevant and the manuscript is jutified. To improve the review, I suggest some changes: -Authors should commented the new treatments for Hepatitis C, not only peginterferon and ribavirin (it seems that they are the only available drugs along the text...). Obviously, the importance of functional food with new DAAs is minor, what should be mentioned too. For this porpose, two references should be added: Ther Adv Infect Dis. 2013 Jun;1(3):107-16 / Aliment Pharmacol Ther. 2014 Apr;39(7):686-98. -In the topic, some essential references have not been included such as "Tomato-based functional food as interferon adjuvant in HCV eradication therapy. J Clin Gastroenterol. 2004 Jul;38(6 Suppl):S118-20." Please, comment this.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	[Y] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Minor revision
[Y] Grade E: Poor		[ ] Existing	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

To search for new natural anti-HCV agents, the authors found a potent inhibitor of HCV RNA expression in the extracts of blueberry leaves and then identified proanthocyanidin as the active ingredient. Proanthocyanidin is an inhibitor of heterogeneous nuclear ribonucleoproteins (hnRNPs) such as hnRNP A2/B1. In this manuscript, the authors presented an overview of functional foods and ingredients efficient for HCV infection, the chemical structural characteristics of proanthocyanidin, and its action mechanism. Although the authors tried to review the effects and mechanisms on hepatitis C virus (HCV) by molecules extracted from natural foods, most of the data were from solitary in vitro studies. In addition, the authors focused on the identification of proanthocyanidin and the action mechanism of proanthocyanidin. Nevertheless, the statements and discussions were only based on one article by the authors (Ref. 13, Takeshita et al, J Biol Chem 2009; 284: 21165). Thus, there is no enough evidence to support this review article.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
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Title: Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism
Reviewer code: 02860871
Science editor: Yue-Li Tian
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Date reviewed: 2014-09-03 22:17

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[Y] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This review titled "Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism" by Ishida et al is interesting in its field. The authors discussed several ingredients with focus on their own previous discovery that blueberry leaves containing active components have anti-HCV activity. It is always interesting to discuss about functional foods for health, since it is an alternative and the more natural way against diseases. Here some comments : 1. The author would better discuss more about foods producing proanthocyanidin since there are many foods contents proanthocyanidin and its oligomer (see USDA Database for the Proanthocyanidin Content of Selected Foods) and explain why author is interested in less common use food, rabbit eye blueberry leaves, because its extract actually exhibited the highest antioxidant activity produced from chlorogenic acid, quercetin and its derivatives content (J Agric Food Chem. 2013 Jan 23;61(3):523-31) and not from proanthocyanidin content. 2. When citing literature about other functional foods inhibit hepatitis C in page 5, emphasize the analytical synthesis of the literatures, not only mentioning who did what. 3. Refrain from quoting other reviews, especially when not necessary. This is a review that needs to be a reference, so original papers need to be cited when making statements (e.g ref 15 & 16) Minor points : a) The term 'proanthocyanidin' in this review refers to oligomer proantocyanidin (OPC), therefore it should be clear mentioned in every sentence using term 'proanthocyanidin' whether it is oligomer or not, because they are functionally different. b) Reference number 35 in page

6 is not relevant to the previous sentence which discussed about health promoting benefits in human. c) Provide reference for "…the most potent activity was observed in the leaves of the rabbit-eye blueberry plant (Vaccinium virgatum Aiton)…" in page 6. d) "hnRNPs comprise a family of RNA-binding proteins…." In page 7 should be rephrased avoiding abbreviation in the early sentence. e) Provide explanation for Figure 4 legend instead of only mentioning in the text manuscript. The flow chart in figure 4 is also not clear enough.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
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Title: Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism
Reviewer code: 02860874
Science editor: Yue-Li Tian
Date sent for review: 2014-08-27 14:18
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This is an interesting review about functional foods that could have a role in hepatitis C. However, along all the article authors emphasize that current therapy is not so affective and with several adverse effects, but they not take in count the novel advances in the field of therapy for hepatitis c, such as protease inhibitors that have less adverse effects and greater sustained virological response. Then, they must restructured their article in order to describe which could be the role for functional foods as a complementary useful agents.

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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology
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Title: Functional foods effective for hepatitis C: identification of proanthocyanidin and its action mechanism
Reviewer code: 01560464
Science editor: Yue-Li Tian
Date sent for review: 2014-08-27 14:18
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[Y] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Existing	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] No records	
[ ] Grade D: Fair	[ ] Grade D: Rejected	BPG Search:	[ ] Rejection
[ ] Grade E: Poor		[ ] Existing	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

1) This review introduced the functional foods and their effective ingredients to modulate various biological processes such as apoptosis and to prevent and treat the cancer. Especially to introduce the proanthocyanidin as the blue berry leaf-derived inhibitor of HCV subgenomic RNA replication and the molecular mechanism underlying the suppression of HCV RNA expression. It is important guidance to well known about the functional foods and their effective ingredients to difficultly prevent and treat the diseases such as cancer, viral hepatitis and so on . 2) I suggest that the article can be published in the form of review in world J Hepatology.