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Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road,
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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7628

Title: Inhibitory effects of dihydromyricetin on the migration and invasion in SK-Hep-1 and MHCC97L cells by down-regulation of matrix metalloproteinase-9 expression

Reviewer code: 00004364

Science editor: Wen, Ling-Ling

Date sent for review: 2013-11-27 20:01

Date reviewed: 2013-12-03 16:19

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Inhibitory effects of dihydromyricetin on the migration and invasion in SK-Hep-1 and MHCC97L cells by down-regulation of matrix metalloproteinase-9 expression In this study, the authors found that Dihydromyricetin (DHM) induced the suppression of migration of HCC lines (SK-Hep1 and MHCC97L). DHM also inhibited production of MMP9 and the activation of MAPK pathways. These findings are novel and of interest, but several experiments are required for publication. Comments 1. In Figure5, they found that protein production of MMP9 is significantly down-regulated by the addition of DHM. However, the activities of these MMPs were regulated by the cleavage of themselves. Thus, it is important to analyze the activities of these MMPs regulated by DHM using gelatin-zymography or other methods. 2. In Figure6, ERK, p38MAPK, JNK, and PKC were regulated by DHM. However, there were no data about the correlation between these signal molecules and cell migration (or MMP production). I recommend that they do the experiment to inhibit these signal molecules using chemical inhibitors in cell migration assays and MMP expression assays.



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ESPS Manuscript NO: 7628

Title: Inhibitory effects of dihydromyricetin on the migration and invasion in SK-Hep-1 and MHCC97L cells by down-regulation of matrix metalloproteinase-9 expression

Reviewer code: 01490296

Science editor: Wen, Ling-Ling

Date sent for review: 2013-11-27 20:01

Date reviewed: 2013-12-19 02:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Li et al. describe in their manuscript the "Inhibitory effects of dihydromyricetin on the migration and invasion in SK-Hep-1 and MHCC97L cells by down-regulation of matrix metalloproteinase-9 expression". - Reference #1 is not appropriate; the authors comment on the prevalence of cancer, reference #1, however, is a review about "Curcumin and liver cancer". Although this review cites original sources for statistics of cancer prevalence, it is not an original source for statistics. Li et al. are advised to use original references, such as publications from the American Cancer Society or similar - English language and grammar have to be improved and corrected throughout the manuscript. - Some formatting is incorrect, e.g. degree centigrade. - Material and Methods: Please give more detailed information on the cell lines used. From what type of hepatic cancer do they derive? - Results 3.1. The authors talk wrongly about the effects of MTT on cell proliferations; the authors should correctly talk about cell viability (as they have correctly indicated on the figure). In addition, the authors should state their rationale to choose the specific range of 5 - 100 μ M. Even 5 μ M appears to be quite high within the physiological context. More detail is needed. - Fig. 2 C/D: It is unclear how exactly the actual cell numbers were obtained. The authors describe in the Material & Methods section that photographs were taken, but they did not state how cells were counted. It appears not to be feasible to count actual cell numbers in light microscopic pictures without any kind of stain, as single cells cannot be distinguished from each other once they grow in close proximity. - Discussion: Give references to both statements "DHM is the principal pharmacological components of *Ampelopsis grossedentata*, which is a traditional Chinese herb used to treat tinea corporis in South China" - Discussion: The authors mention in the discussion "... , we found DHM could not inhibit the



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viability of hepatic L02 cells, an immortalized nontumorigenic normal human hepatocyte cell line (data not shown)". This information is quite relevant, and data should be included in the Result and Material & Methods section.



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Title: Inhibitory effects of dihydromyricetin on the migration and invasion in SK-Hep-1 and MHCC97L cells by down-regulation of matrix metalloproteinase-9 expression

Reviewer code: 02445986

Science editor: Wen, Ling-Ling

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The author's review manuscript indicates that DHM can lead to suppression of HCC migration and invasion. DHM decreased the expression of MMP-9, p38 and JNK in a concentration-dependent manner. However, p38, JNK and ERK1/2 are widely expressed protein kinase intracellular signaling molecules that are involved in functions including the regulation of meiosis, mitosis in differentiated cells. Decreasing those signals will effect to cell proliferation. However, MTT assay result indicated that DHM did not effect HCC proliferation. The method of MTT assay did not follow general methods. However, author's manuscript is well organized, interesting and suitable for publication. Major comments In the material and methods, the method of MTT assay was not executed properly. After incubation of cells with MTT, the formazan crystals were formed in the culture dish. If the media is removed from the culture dish, MTT and formazan crystals are removed. Please check to experimental methods and compare with industrial or previous reported methods. Also, a negative control is needed, such as 0.5% BSA without FBS. Minor comments Temperature symbol did not show in contents.