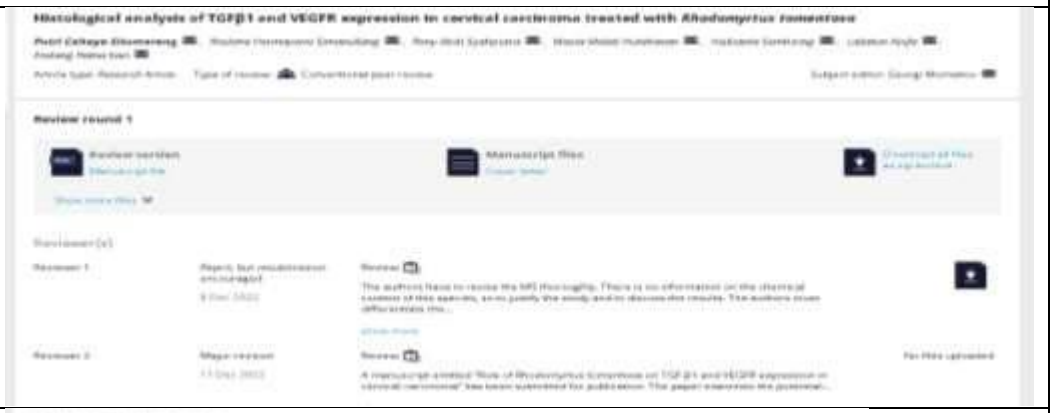
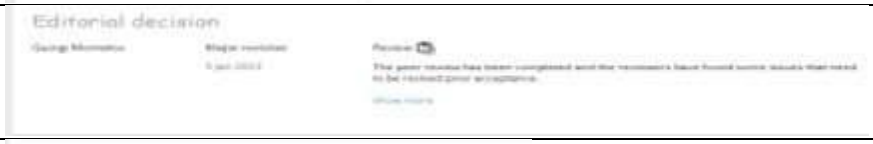
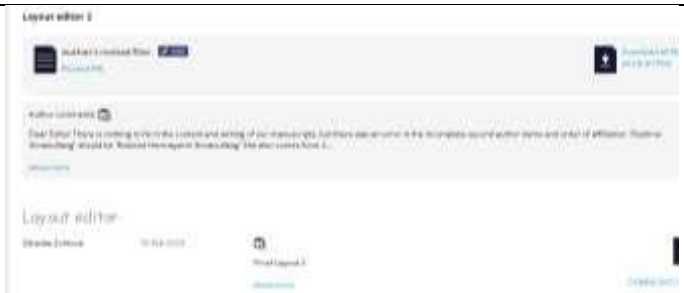
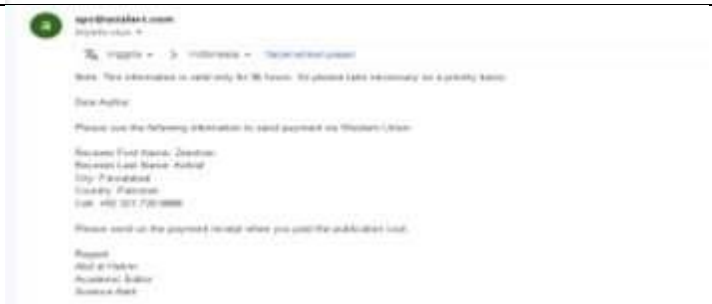
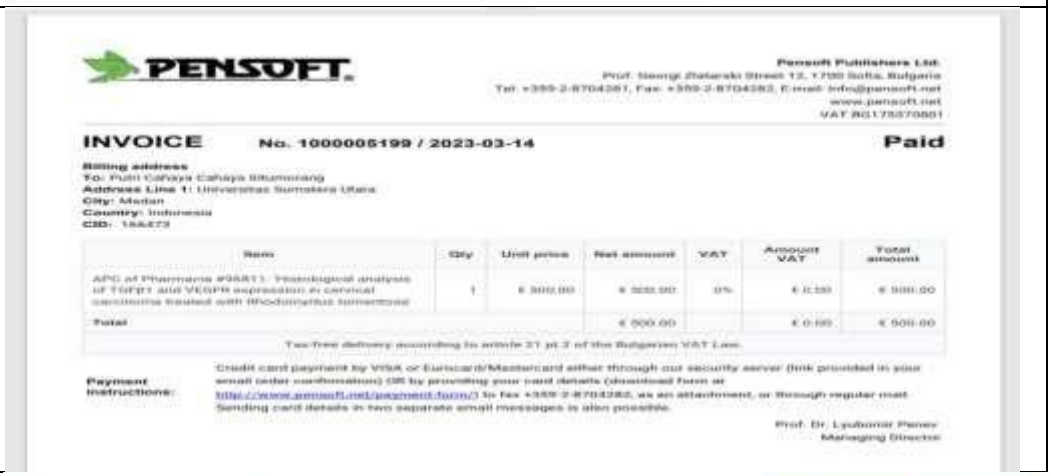
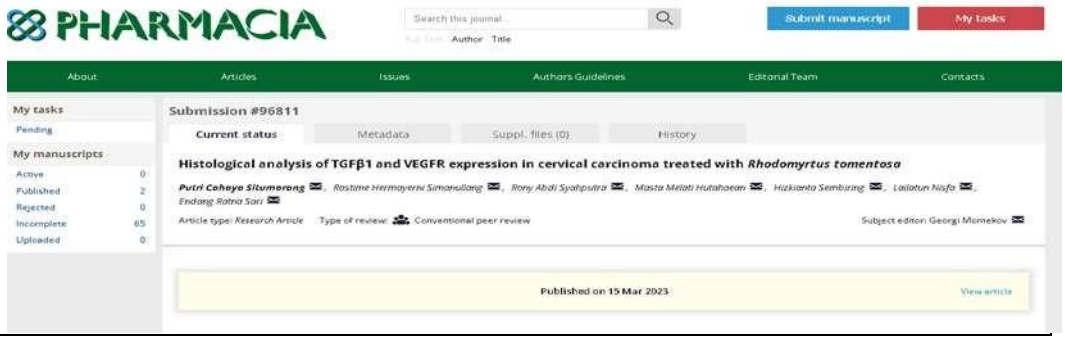
Judul		Histological analysis of TGFβ1 and VEGFR expression in cervical carcinoma treated with Rhodomyrtus tomentosa.
Nama Jurnal/Volume/issu/Hal		Pharmacia 70 (1): 217–223
Peran		Co-Author
No	**Tanggal**	**Keterangan**
1	22-11-22	Submission
2	22-11-22	Koreksi oleh reviewer
3	08-12-22	Koreksi oleh reviewer
4	11-12-22	Pengiriman revisi sesuai instruksi
5	05-01-23	Instruksi melengkapi kembali revisi yang diminta
6	17-01-23	Accepted
7	10-02-23	Copy editing
8	15-02-23	Instruksi proof reading dan last editing
9	16-02-23	Pengiriman revisi terakhir dan permintaan pembayaran
10	14-03-23	Pembayaran manuscript
11	15-03-23	Published

Waktu	Bukti Korespondensi
22-11-22	Submission
08-12-22 11-12-22	
05-01-23	
17-01-23	
10-02-23	
15-02-23	

16-02-23	
27-02-23	
14-03-23	
15-03-23	

PENSOFT.

Pensoft Publishers Ltd.
Prof. Georgi Zlatarski Street 12, 1700 Sofia, Bulgaria
Tel: +359-2-8704281, Fax: +359-2-8704282, E-mail: info@pensoft.net
www.pensoft.net
VAT BG175370801

INVOICE No. 1000005199 / 2023-03-14 **Paid**

Billing address
To: Putri Cahaya Cahaya Situmorang
Address Line 1: Universitas Sumatera Utara
City: Medan
Country: Indonesia
CID: 184473

Item	Qty	Unit price	Net amount	VAT	Amount VAT	Total amount
APC of Pharmacia #96811: Histological analysis of TGFβ1 and VEGFR expression in cervical carcinoma treated with Rhodomyrtus tomentosa	1	€ 500.00	€ 500.00	0%	€ 0.00	€ 500.00
Total			€ 500.00		€ 0.00	€ 500.00

Tax-free delivery according to article 21 pt 2 of the Bulgarian VAT Law.

Payment instructions: Credit card payment by VISA or Eurocard/Mastercard either through our security server (link provided in your email order confirmation) OR by providing your card details (download form at http://www.pensoft.net/payment-form/) to fax +359-2-8704282, as an attachment, or through regular mail. Sending card details in two separate email messages is also possible.

Prof. Dr. Lyubomir Penev
Managing Director

PHARMACIA

Search this journal
Author Title

Submit manuscript | My tasks

About | Articles | Issues | Authors Guidelines | Editorial Team | Contacts

My tasks
Pending

My manuscripts
Active 0
Published 2
Rejected 0
Incomplete 65
Uploaded 0

Submission #96811

Current status | Metadata | Suppl. files (0) | History

Histological analysis of TGFβ1 and VEGFR expression in cervical carcinoma treated with *Rhodomyrtus tomentosa*

Putri Cahaya Situmorang, *Rostime Hermayerni Simanullang*, *Rony Abdi Syahputra*, *Masta Melati Hutahaean*, *Hizkianto Sembiring*, *Lailatun Nisfa*, *Endang Ratna Sari*

Article type: *Research Article* Type of review: Conventional peer review Subject editor: Georgi Momekov

Published on 15 Mar 2023 View article

Clarification for reviewer's comments.

Tittle: **Histological analysis of TGFβ1 and VEGFR expression in cervical carcinoma treated with *Rhodomyrtus tomentosa***

No	Part	Reviewer'scomment	Author's comment
1	Title	**Do the title, abstract and keywords accurately reflect the content of the manuscript and underlying data?** Moderately	We changed our title to " **Histological analysis of TGFβ1 and VEGFR expression in cervical carcinoma treated with *Rhodomyrtus tomentosa"***
	Material and methods	The authors must differentiate the plant species and the extract. In each case, the extract should be indentified as such, maybe with an abbreviation. I**t is not the same to treat animals with the whole plant, as it is written - roots, leaves, stems, etc, and the animals to be treated wit a specified extract from a specific plant organ.** This is a major drawback.	We have fixed it, please find it in the material and method section
	Material and methods	The plant material, the extraction procedure are missing. This makes the study unreproduicible.	We have revised it Preparation: The leaves and twigs of *R. tomentosa* were separated. The leaves were cleansed of any soil or dust that adhered to them, and they were dried for 7 days at room temperature and smoothed. Extraction: 500 grams of *R. tomentosa* dry powder were macerated in 96% technical ethanol for 24 hours at room temperature. Maceration with a 96% technical ethanol solvent yielded the ethanol extract of *R. tomentosa.* The maceration products were filtered using a Buchner funnel and a vacuum pump. Using the same method, the filtered residue was macerated twice more. A rotary evaporator was used to concentrate the ethanol extract, which was then dried for 8 hours to produce a solid ethanol extract. Production of micro-colloidal *R. tomentosa* (CER): An ethanol

			extract of the leaves was prepared by sonication as follows: 0.5 mg of *R. tomentosa* extract was added to a Tween 20 solution. Capryol 90 was added, and the solution was homogenised. PEG-400 was added, and the solution was sonicated. The prepared substance was dissolved in distilled water (1:100) and sonicated with an ultrasonic device (Sonicator Ultrasonic Homogenizers and Emulsifiers), and the micro-colloidal *R. tomentosa* (MR) was ready for use in animals experiments.
	Material and methods	There is no information on: the animal husbandry; the route of administration of the supposed extract; how the animals were sactificed; how the doses used were chosen.	*R. tomentosa* leaf ethanol extract was administered for 30 days orally. The dose was in accordance with the acute toxicity test and previous studies (Situmorang *et al.,* 2021, 2022a, 2022b). The animals was euthanized with administering an anaesthetic combination of 300 mg/kg BW of ketamine and 15–30 mg/kg BW of xylazine was administered then rats were dissected for taken the cervix
	Material and methods	There is some misunderstanding in the methodology. The authors should explain the experimental modell better. How do you interpretate the statement: "A bulge was then ignored for three months **until it was thought to be a malignancy**." How is it possible to thought that this is malignancy?	The rats were injected vaginally with 50 mg of benzopyrene diluted with corn oil. The tumour was identified when a lump was found due to administration of benzopyrene for three months, and samples were sent to the Anatomical Pathology Laboratory of the USU to ensure that the tissue was tumorous.
	Material and methods	How is it technically possible the following: "**The blood serum was homogenized in a homogenizer tissue** for 5 minutes with 10 ml of PBS pH 7.4, **the supernatant was collected**, and the levels of SOD and MDA were determined using an ELISA reader at 450 nm." How a serum is homogenised with a tissue homogenizer and how a supernatant	**Measurement of *superoxide dismutase*** Superoxide dismutase (SOD) analysis was performed using the blood of the rats with cervical cancer. The Superoxide Dismutase Activity Kit was used to measure SOD activity. After dilution with a uniquely colored sample diluent, the sample is

		was obtained from that? Which reactions and reagents were used?	loaded into wells. Xanthine oxidase reagent was added after the substrate, and the mixture was allowed to sit at room temperature for 20 minutes. In the presence of oxygen, xanthine oxidase generates superoxide, which converts the colourless substrate in the detection reagent to a yellow product that is detectable at 450 nm. **Measurement of malondialdehyde** Blood plasma samples from the rats were assessed with traditional thiobarbituric reactive species spectrophotometry (TBARS). The Malondialdehyde (MDA) Assay Kit (competitive enzyme-linked immunosorbent assay) (ab238537) was used for rapid detection and quantification of the protein MDA. This kit enables the quantification of MDA addition in a determined protein sample by comparing its absorbance with a known MDA-BSA standard curve. Then, the MDA-TBA2 condensation product can be measured via UV-VIS spectrophotometry.
	Figure	In the figures the legends are quite confusing - each figure is consisted of 6 pannels, lettered a-f, but the caption is written as a whole. It is not possible to decide which pannel is for which group.	We have revised it
	All pages	Many sentences throughout the document require serious English revision, as they are poorly constructed, lack a verb or subject and make no sense. Lexical inaccuracies are also an issue. For example: **“**Utilizing natural herbs in molecular therapy for cervical cancer can be treated.” “Given that it accounts for half of all malignant tumors that develop in the female reproductive system. “ “It has been demonstrated that this plant's rhodomyrtone content	We have sent our manuscript to native English. Please find a proof certificate in this bellow!.

		inhibits cell migration, adhesion, and A431 cell invasion as well as **acting** as a new therapeutic agent to stop cancer metastasis." "The rats were given Rhodomyrtus tomentosa for **1 month after 3 months**, and then they were dissected to collect the tumor tissue." "The blood serum was homogenized in a **homogenizer tissue** for 5 minutes…" "Slices of **Cervical** that had been embedded…" "TGF-1 monoclonal antibody, catalog #MA1-169 (B11-4C3); VEGFR1 (soluble) polyclonal antibody, catalog #36-1100; and Antigen Affinity-purified Polyclonal Antibody **were treated with tissue slices**", etc.	
	All pages	The sentence: *"Increased TGFβ1 production is also linked to cervical cancer, which implies that gene inactivation contributes to the emergence of cervical carcinoma.*" carries a contradictory statement regarding the effect of TGFβ1 on the neoplastic process. A further discussion of the cytokine's bias role as a tumor promoter or suppressor in the context of the experimental results is recommended.	We have sent our manuscript to native English. Please find a proof certificate in this bellow!.
	Material and methods	administered to **five** rat groups: The Rhodomyrtus tomentosa 100mg/BW group, Rhodomyrtus tomentosa 200mg/BW group, Rhodomyrtus tomentosa 400mg/BW group, Group C- is the control group, Group C+ is the cancer model group, and Group CER100 is the Rhodomyrtus tomentosa group". Treated groups are not five (excluding both controls), and what does the latest group represent (is it not the same as Rhodomyrtus tomentosa 100mg/BW group)?	We have revised it
	Figures	1. Images in **Figure 1a** and **1b** are of very poor quality. In the same figure,	We have revised it

		the five experimental groups lack assignment to the correspondent images “a” through “e”. What do the red arrows point to? You cannot directly relate to TGFβ1 expression levels in a light microscopic image. 2. The same goes for **Figure 2** (no image assignment, VEGF expression can be addressed only in the context of tissue vascularization).	
	Discussion	the authors refer to rhodomyrtone as a key component in Rhodomyrtus tomentosa extracts and its biological activity. Perhaps the authors should consider measuring its content in the extract or using it as a reference compound.	We have added that Antioxidants have been shown to reduce toxic side effects during cancer treatment (Situmorang et al., 2021). Antioxidant-containing plants, such as R. tomentosa, have been associated with cancer treatment with few side effects.). Previous studies have analysed the content of *R. tomentosa*, which contains high levels of antioxidants in nano- or micro-colloid sizes and has low toxicity (Situmorang *et al.*, 2021; Simanullang *et al.,* 2022a).

Certificate of Proofreading

CAMBRIDGE Proofreading & EDITING LLC

EDITING CERTIFICATE

This document certifies that the manuscript listed below was edited by Cambridge Proofreading LLC for English grammar, punctuation, spelling, and style. We endeavoured to ensure that the authors' intended meaning was not altered during the review. All amendments were tracked with Microsoft Word's 'Track Changes' feature, allowing the authors full control over the changes made. We bear no responsibility for revisions made to the document after our edit on the date listed below.

Document title:

Histological analysis of TGFβ1 and VEGFR expression in cervical carcinoma treated with *Rhodomyrtus tomentosa* extract

Document authors:

Rostime Hermayerni Simanullang and Putri Cahaya Situmorang

Date edited: 07/01/2023

Order number: 744-34-77

For queries or verification contact info@cambridgeproofreading.com

Cambridge Proofreading LLC is a registered company headquartered in Chicago, Illinois, with a global presence. Our Certificate of Good Standing can be found in the Illinois state business database.