

Current Pharmaceutical Analysis

Manuscript Evaluation Form

Editor-in-Chief: Anastasios Economou, Department of Chemistry, Laboratory of Analytical Chemistry, University of Athens, Athens, Greece

PAPER TITLE	Pharmacokinetic differences of grape seed procyanidin by gavage administration between Alzheimer's Disease and normal in rats
AUTHOR(S) NAME	Xinhui Cheng, Jingying Zhang, Huiting Jing, Yu Qi, Tingxu Yan, Bo Wu, Yiyang Du, Feng Xiao, Ying Jia

Sec. A: REFEREE'S ASSESSMENT

(cross as appropriate)

Criterion	Excellent	Good	Fair	Poor
Originality of the topic	x			
Technical Quality		x		
Importance in its Field	x			
Style & Overall Representation		x		
Readily Understandable	x			
Suitability for the Journal	x			
Adequate Illustrations or Drawings	x			
English language		x		
Description	Yes	No	Comments/ Suggestions	
Does the title represent manuscript's contents?	x			
Is the Abstract accurate and concise?	x			
Are the approach/ methods properly described?	x			
Are the conclusions and interpretations sound?	x			
Are the references properly cited?	x			
Is this a new/ original/ contribution?	x			
Is it within the scope of the journal?	x			
Overall the Paper is Rated:	(Excellent ----- Poor) 10 9 8 7 6 5 4 3 2 1			

Sec. B: REFEREE'S RECOMMENDATIONS

OTHER SPECIFIC CRITICISMS

Accept with minor changes

x

Imperfect style

Accept with major changes

Too long

Reject in current form, but may be resubmitted

References incorrectly presented

Reject, with no resubmission

Typographical and Grammatical errors

x

PAPER TYPE: Research article

Review article

Letter article

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Confidential Comments to the Editor (not for Transmission to Authors):

The article is within the scope of the journal and suitable for publication after some revision.

Comments for the Authors (continue on another sheet, if necessary):

Review of the article entitled

Pharmacokinetic differences of grape seed procyanidin by gavage administration between Alzheimer's Disease and normal in rats, by Xinhui Cheng, Jingying Zhang, Huiting Jing, Yu Qi, Tingxu Yan, Bo Wu, Yiyang Du, Feng Xiao, Ying Jia

This article investigates the possible pharmacokinetic differences of grape seed procyanidins (GSP) between Alzheimer's disease (AD) and normal rats. A rapid ultra performance liquid chromatography – tandem mass spectrometry (UPLC-MS/MS) method for detecting their content in plasma samples was established, and the plasma concentrations of procyanidin B₂, procyanidin B₃, catechin and epicatechin were analyzed in normal and AD rats over time. It was found that the absorptions of these analytes in AD group are better than in normal group, which provides an analytical basis for the treatment of AD with procyanidins.

The article is within the scope of the journal and suitable for publication after some revision.

The English language has to be improved.

For example, in the title of the article state: Pharmacokinetic differences of grape seed procyanidins by gavage administration between Alzheimer's disease and normal rats

Use plural for grape seed procyanidins and consequently in the entire sentences within the manuscript where they are mentioned, including captions of Tables 1, 2 and 3, as well as legend of Fig 5, extract of procyanidins
In the abstract, background, Grape seed procyanidins (GSP) are a kind of natural polyphenols

In the Results of the abstract, use the Past Tense in the entire sentence, could be seen, instead of can be seen

In Conclusion, We found that the absorptions of these analytes in AD group is better than in normal group, which provides an analytical basis for the treatment of AD with procyanidins.

In the Introduction, page 3, As a result of the in-depth study of procyanidins, some researchers found that procyanidins have stronger anti-oxidative and free radicals scavenging abilities, because of containing many electronic hydroxyl portions.

Studies *in vivo* have also shown that those abilities of procyanidins are stronger compared to vitamin C and vitamin E.

Besides the classic β -Amyloid (A β) and the Tau protein phosphorylation hypothesis, another one is due to the oxidative stress in the brain of AD patients.

Some researchers have shown that procyanidins can inhibit the production of A β , which can reduce the A β -induced neurotoxicity, playing a neuroprotective role.

Growing research suggests that grapes and wines have beneficial effects for human health, which also confirms that procyanidins have a positive effect on chronic, neurodegenerative and cardiovascular diseases.

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On page 4, in the third sentence use italic for *in vitro*

The last sentence on this page should be: The aim of this research was to investigate the possible pharmacokinetic differences between GSP in control and AD rats, to fill the pharmacokinetic gap of GSP in normal and AD mice and also to compare the *in vitro* content of procyanidins with the utilization *in vivo*, in order to better study the procyanidins and improve the main components of AD.

On page 5, correct the spelling in heading 2. Materials and methods

Begin the third sentence with the capital letter: Ultrapure water equipment

The collected plasma was placed in the 1.5 mL EP tube of heparinization.

The mobile phase consisted of:

Replace point, instead of ; at the end of the third sentence.

The correct spelling is Quadruple, instead of Quadrupole

Begin the sentence with the capital letter: Capillary voltage was 3.5 kV;

On page 6, UPLC was used with methanol-0.1% phosphoric acid solution as mobile phase

A series of mixed working standards was prepared, having 4–10,000 ng·mL⁻¹ for procyanidin B₂ and epicatechin, 3–8000 ng·mL⁻¹ for procyanidin B₃, 5–12,000 ng·mL⁻¹ for catechin

The stock solutions were then serially diluted with methanol.

Quality Control (QC) samples:

On page 7, place in the same row ML: ± 2.2 mm, and in the next row DV: –3.0 mm

Move subheading 2.7.1. to the next page

On page 8, use comma before, analyzing five sources of 100 µL blank rat plasma without internal standard.

The calibration curves were prepared and were established

A least squares linear regression method (1/x²)

Use the capital letter at the beginning of subheading

2.7.3. Lower limit of quantification (LLOQ)

its accuracy should be achieved between ~ 80-120 % of the true concentration

In the last paragraph, the standard peak areas of the analytes, instead of often

On page 11, in the legend of Fig. 2, correct spelling, blank plasma sample of normal (A), instead of norma (A)

On page 12, move to the next page subheading 3.2.3.

On page 13, the last sentence of the first paragraph should be: The presented results show that the method has good precision and accuracy.

The extraction recovery rate and matrix effect of procyanidins are shown in Table 1. It can be seen that the extraction recovery rates of procyanidin B₂, procyanidin B₃, catechin, and epicatechin range from 95% to 85%, which conforms to the requirements of *in vivo* analysis.

In the caption of Table 1, state: The extraction recovery and matrix effect of procyanidins in different samples.

The accuracy and precision of the analytical method (n = 6).

On page 14, this does verify that the method is suitable for the routine pharmacokinetic analysis.

Table 2 Stability of procyanidins assay (n = 6).

On page 15, end the first sentence with the point, instead of comma,

Subheading should be

3.5. Comparison of pharmacokinetics of procyanidins in AD and control rats

State: the pharmacokinetic parameters of procyanidins (procyanidin B₂, procyanidin B₃, catechin, epicatechin) in rats are shown in Table 3, and the average plasma concentration time curves are shown in Fig. 5.

End the paragraph with: , indicating that GSP have more favorable absorption and slower elimination characteristics in the AD group.

Page 16, Table 3 Pharmacokinetic parameters of procyanidins in AD rats, *P < 0.05 compared with control group (mean ± SD; n = 6).

On page 17, It was found in the study of GSP that they are very stable in the gastrointestinal environment.

On page 18, significant degradation occurs

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Therefore, regulation of intestinal flora may be one of the mechanisms by which GSP impact metabolic health

Use italic for *in vitro*

In conclusion, and provides new ideas

Use small letter for: and it could be used as a potential drug, or begin a new sentence with It could be used

On page 19, correct words, such as participate, University animal experiment center guidelines, experiments, Experimentation

Use one space between the numbers and units of measure in the entire manuscript.

Use space between the adequate words and numbers or symbols in the manuscript, and delete the additional spaces at some places.

State the complete term and the abbreviation at the first place where it appears, in the rest of the text use either the abbreviation or full term.

Delete the points after the captions of Tables and format the entire manuscript according to the style of the journal.

Add the numbers of issues to the references 6, 7, 9, 11-13, 21, 27 and 28, if available.

FIELD OF EXPERTISE OF REFEREE: Materials and chemical technologies, nanotechnologies, biomedical engineering, chemistry, medicinal and pharmaceutical chemistry

Name & Affiliation of referee: Tamara Jovanovic, Department of Biomedical Engineering, Faculty of Mechanical Engineering, University of Belgrade, Kraljice Marije 16, 11120 Belgrade, Serbia

Dr Tamara Jovanovic / April 25, 2019

SIGNATURE OF REFEREE / DATE

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