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OPEN PEER REVIEW

A Natural Additive Alternative to the Cosmetics Industry: Hazelnut and Its Waste Products

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About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

3 comments · 27 May 2023 – 29 May 2023

Referee 1 Reviewer

MINOR REVISION 27 May 2023

Dear AE,
I thank the authors and express my appreciation to the researchers. The manuscript is a valuable piece of research. But some revisions are needed.
ABSTRACT:
1- The study design should be mentioned in the first line of the method section of the ABSTRACT.
2- A summary of the statistical analysis results should be mentioned in the result section of the ABSTRACT.
3- It would be helpful to provide a brief discussion of the implications and potential applications of using hazelnut and its by-products as natural bioactive agents in the cosmetics industry.

TEXT:
Background:
Some sentences lack references. It would be beneficial to briefly mention the potential economic and environmental benefits of utilizing hazelnut waste products, as this aligns with the aim of preventing environmental pollution, supporting the hazelnut economy, and increasing interest in hazelnuts.

Method:
Moreover, it is recommended to provide more details about the spectrophotometric measurements conducted for determining SPF values, such as the specific wavelengths used and any standardization procedures followed. This would ensure transparency and facilitate accurate interpretation of the results. Additionally, it would be helpful to include information about the concentration of the hazelnut extracts and the probiotic strain used in the cream formulations, as well as any considerations regarding their compatibility and stability within the cream matrix.

REFERENCES:
Some references are old. Please replace them with recent studies.

Associate Editor

MINOR REVISION 29 May 2023

Dear EIC,
This study is useful research but needs some revision. The authors should respond to all comments and make changes based on the comments.

Editor-in-Chief

MINOR REVISION 29 May 2023

Dear Author,
Thank you for submitting the article. It needs some revision. Please revise it based on the reviewers' and AE's comments.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Title: A NATURAL ADDITIVE ALTERNATIVE TO THE COSMETICS INDUSTRY: HAZELNUT AND ITS WASTE PRODUCTS

Id: 137580

Article Type: Research Paper

Dear Editor,

We would like to express our gratification for the opportunity to improve the paper and appreciate your guidance. We have tried our best to ensure the required revising corrections.

We, here, have listed the comment and our response to them point-by-point.

We are looking forward to hearing from you at your convenience.

Yours sincerely,

Prof. Dr. Meltem ASAN OZUSAGLAM

COMMENTS AND AUTHOR'S RESPONSE

REVIEWER 1

Abstract:

1. Study design should be mentioned in first line of method section of ABSTRACT.

Our response: Thank you very much for comment. In the method section of the abstract, the study design was mentioned and the relevant sentences were rearranged. Changes are marked in red.

Methods: The extracts of hazelnut whole fruit (with brown shell), green husk (green leafy shell) and leaves were obtained separately using water and methanol solvents. Firstly, disc diffusion assay was applied to evaluate the antimicrobial potential of the extracts. The minimal inhibition (MIC) and minimal bactericidal (MBC) or fungicidal (MFC) concentrations of the extracts were also determined. Then, the sun protection factor (SPF) of the extracts and commercial cream+extract mixtures were determined in vitro. Additionally, antimicrobial cream formulations containing hazelnut extracts and *L. fermentum* MA-7 probiotic candidate lactic acid bacteria from human milk have been developed for the pharmaceutical industry. The well diffusion test was applied against the test microorganisms to evaluate the antimicrobial activity of the developed antimicrobial cream formulations.

2. Summary of Statistical analysis results should be mention in result section of ABSTRACT.

Our response: A summary of the statistical analysis results has been added to the conclusion section of the summary. Added sentences are marked in red.

…The results of *statistical* analysis indicated that the cream+extract+probiotic pellet+probiotic supernatant (CEPS) group was found statistically significant ($P<0.05$) compared to other test groups.

3. It would be helpful to provide a brief discussion of the implications and potential applications of using hazelnut and its by-products as natural bioactive agents in the cosmetics industry.

Our response: Information about the effects and potential applications of hazelnuts and their by-products in the cosmetic industry are given in the sentences below.

Conclusions: The results showed that hazelnuts and their by-products have the potential to be used as a natural source of antimicrobials. Hazelnut and its by-products can be an alternative to synthetic antimicrobials and sunscreens in the cosmetic industry as a natural bioactive substance. In addition, it may be possible to contribute to the country's economy by evaluating hazelnuts and their waste and by-products resulting from their processing in the cosmetic industry.

Text:

4. Some sentences are without reference. It would be beneficial to briefly mention the potential economic and environmental benefits of utilizing hazelnut waste products, as this aligns with the aim of preventing environmental pollution and increasing the economy and interest of hazelnuts.

Our response: The new references have been added to the non-referenced sentences in the background. In addition, the economic and environmental benefits of the use of hazelnut waste products are mentioned.

Added references:

- Vlahova V. The role of hazelnuts (*Corylus Avellana* L.) for the sustainability of the agroecosystem. *New Knowledge Journal of science*. 2020;**9**(4): 77-84.
- Wang Z, Koirala B, Hernandez Y, Zimmerman M, Park S, Perlin DS., et al. A naturally inspired antibiotic to target multidrug-resistant pathogens. *Nature*. 2022;**601**(7894): 606-611.
- Gideon M, & Ladan Z. Synergistic combinatorial strategy for combating Antimicrobial Resistance (AMR) in clinical bacteria by combining antibiotics with plant extracts. *Fine Chemical Engineering*. 2023;**4**(1): 1-12.
- Mondal H, & Thomas J. A review on the recent advances and application of vaccines against fish pathogens in aquaculture. *Aquaculture International*. 2022;**30**(4): 1971-2000.

…Thus, the importance of hazelnut production worldwide can be increased by the development of new alternatives for the use of hazelnuts and their wastes as bioactive substances in the cosmetic industry.

Method:

5. Moreover, it is recommended to provide more details about the spectrophotometric measurements conducted for determining SPF values, such as the specific wavelengths used and any standardization procedures followed. This would ensure transparency and facilitate accurate interpretation of the results. Additionally, it would be helpful to include information about the concentration of the hazelnut extracts and the probiotic strain used in the cream formulations, as well as any considerations taken regarding their compatibility and stability within the cream matrix.

Our response: The details have been added to the method of determining SPF. The changes are marked with red.

Sun Protection Factor (SPF) values of hazelnut extracts are based on in vitro determination of extracts (2 µg/µL) diluted in ethanol (96%). The diluted solutions were measured in a spectrophotometer (Beckman Coulter) in the wavelength range of 290-320 nm (UV-B) at 5 nm intervals. The SPF value was calculated using the Mansur equation (28) given below [1].

…Commercial cream (10% w/v) and the extract (5% w/v) were mixed and made up to final volume with distilled water. …The SPF values of the cream and extract mixtures were calculated using the Mansur equation (28) given below [1].

… The *L. fermentum* MA-7 strain has good probiotic properties (32). …The extract concentration of all groups containing extract was 200 µg/µL.

References:

6. Some references are old. please replace them with recent studies.

Our response: Old references have been replaced by current studies. The added current studies are listed below.

- Vlahova V. The role of hazelnuts (*Corylus Avellana* L.) for the sustainability of the agroecosystem. *New Knowledge Journal of science*. 2020;**9**(4): 77-84.
- Spagnuolo L, Della Posta S, Fanali C, Dugo L, De Gara L. Antioxidant and Antiglycation Effects of Polyphenol Compounds Extracted from Hazelnut Skin on Advanced Glycation End-Products (AGEs) Formation. *Antioxidants*. 2021;**10**: 424.
- Haş IM, Teleky BE, Szabo K, Simon E, Ranga F, Diaconeasa ZM, et al. Bioactive Potential of Elderberry (*Sambucus nigra* L.): Antioxidant, Antimicrobial Activity, Bioaccessibility and Prebiotic Potential. *Molecules*. 2023;**28**(7): 3099.
- Khonthun C, Khoothiam K, Chumphukam O, Thongboontho R, Oonlao P, Nuntaboon P, et al. Screening and characterization of antioxidant, anti-aging, andanti-microbial activity of herbal extracts. *Functional Foods in Health and Disease*. 2023;**13**(2): 52-68.
- Westover C, Rahmatulloev S, Danko D, Afshin EE, O'Hara NB, Ounit R, et al. Ozone Disinfection for Elimination of Bacteria and Degradation of SARS-CoV2 RNA for Medical Environments. *Genes*. 2023;**14**(1): 85.
- Mateescu MC, Grigorescu S, Socea B, Bloanca V, & Grigorescu OD. Contribution to the Personalized Management of the Nosocomial Infections: A New Paradigm Regarding the Influence of the Community Microbial Environment on the Incidence of the Healthcare-Associated Infections (HAI) in Emergency Hospital Surgical Departments. *Journal of Personalized Medicine*. 2023;**13**(2): 210.
- Ahmad S, Shabbir A, Tareen N, Ahmad S, & Chohan MA. Plant-Derived bioactive compounds as skin photo protection Agents. *International Journal of Natural Medicine and Health Sciences*. 2022;**1**(2).

REVIEWER 2

1. There are some typographic and grammatic errors that should be addressed.

Our response: The manuscript has been revised and corrections have been made. The changes are marked in red.

- …Scientists have proven the medicinal effect of plant-based products on microorganisms (14, 15).
- …Nosocomial infections are one of the serious health problems caused by clinically pathogenic microorganisms despite sterilization and disinfection precautions (17).
- …Plants can produce compounds with many biological activities effective against pathogens. Thus, plant extracts are expected to be effective on drug-resistant pathogenic microorganisms (22).
- …UV radiation, with wavelength energy of 100-400 nm, spans between the x-ray and visible light spectrum. These rays are UV-A, UV-B and UV-C. The ozone layer absorbs 100% of UV-C, approximately 90% of UV-B and almost does not absorb UV-A (24).
- …Using sunscreen products can prevent the skin from the harmful effects of UV rays and the negative skin effects (26).
- The antimicrobial activity of water and methanol extracts from WHF, HH and HL was tested against ten pathogenic microorganisms
- … Then, the microbial suspensions (100 µL) were spread on the solid medium.
- …The plates were then incubated at 37°C for 24 hours for bacterial strains and 48 hours at 30°C for yeast.

- $SPF = CF \, x \sum_{290}^{320} EE(\lambda) \, x \, I(\lambda) \, x \, |(|\lambda)$ [1]

- …The plates were incubated at appropriate conditions as mentioned before.
- …The hazelnut extracts showed antimicrobial activity against most of the tested microorganisms (Table 2).
- … Oğuzkan et al. (38) tested the antimicrobial activity of hazelnut husk (green leafy shell) and hazelnut leaf extracts extracted with methanol on test bacteria.
- … In the current study, the all hazelnut extracts showed antibacterial activity on *E. coli* O157:H7 except for HLW extract.
- …While antimicrobial activity was not detected against *E. coli* O157:H7 in the HLW extract (100 mg/mL) in the disc diffusion test, a higher concentration of the extract (200 mg/mL) used to determine the antimicrobial activity of cream formulations may have created an inhibition zone.

2. The keywords should be according to the Mesh.

Our response: Keywords are arranged as follows.

Keywords: Antimicrobial, Cream formulation, Extract, Probiotic, Solar protection

3. The references are too old.

Our response: Old sources have been replaced by current studies. Added current studies are listed below.

Vlahova V. The role of hazelnuts (*Corylus Avellana* L.) for the sustainability of the agroecosystem. *New Knowledge Journal of science*. 2020;**9**(4): 77-84.
Spagnuolo L, Della Posta S, Fanali C, Dugo L, De Gara L, Gugliucci A. Antioxidant and Antiglycation Effects of Polyphenol Compounds Extracted from Hazelnut Skin on Advanced Glycation End-Products (AGEs) Formation. *Antioxidants*. 2021;**10**: 424.
Haş IM, Teleky BE, Szabo K, Simon E, Ranga F, Diaconeasa ZM, et al. Bioactive Potential of Elderberry (*Sambucus nigra* L.): Antioxidant, Antimicrobial Activity, Bioaccessibility and Prebiotic Potential. *Molecules*. 2023;**28**(7): 3099.
Khonthun C, Khoothiam K, Chumphukam O, Thongboontho R, Oonlao P, Nuntaboon P, et al. Screening and characterization of antioxidant, anti-aging, andanti-microbial activity of herbal extracts. *Functional Foods in Health and Disease*. 2023;**13**(2): 52-68.
Westover C, Rahmatulloev S, Danko D, Afshin EE, O'Hara NB, Ounit R, et al. Ozone Disinfection for Elimination of Bacteria and Degradation of SARS-CoV2 RNA for Medical Environments. *Genes*. 2023;**14**(1): 85.
Mateescu MC, Grigorescu S, Socea B, Bloanca V, & Grigorescu OD. Contribution to the Personalized Management of the Nosocomial Infections: A New Paradigm Regarding the Influence of the Community Microbial Environment on the Incidence of the Healthcare-Associated Infections (HAI) in Emergency Hospital Surgical Departments. *Journal of Personalized Medicine*. 2023;**13**(2): 210.
Ahmad S, Shabbir A, Tareen N, Ahmad S, & Chohan MA. Plant-Derived bioactive compounds as skin photo protection Agents. *International Journal of Natural Medicine and Health Sciences*. 2022;**1**(2).

2 Revision 1

3 comments · 7 Jun 2023 – 10 Jun 2023

Referee 1 Reviewer

MINOR REVISION 7 Jun 2023

Dear AE,
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated. Most of the revisions were completed successfully, but I think the authors misunderstood the study design in the first line of the abstract. The authors should delete the sentences that were added during revision. The authors should mention only the study design (just a few words).
The authors can find their study design in the list below:

Case-Control Study
Case Report or Case Series
Cohort Study
Cross-Sectional Study
Diagnostic Test accuracy Study
Meta-Analysis Study
Systematic Review (with or without a meta-analysis)
Observational Studies in Nutritional Epidemiology
Prediction Model Development/Validation
Randomized Trial Study
Abstract of Randomized Trials
Study using Laboratory Animals
Protocol of a Clinical Trial
Protocol of a Systematic Review and Meta-Analysis
Qualitative Study
Economic Evaluation of Health interventions
Quality Improvement in Health Care
Randomized Trial of a social or psychological intervention
Behavioral and Public Health Interventions
Genetic Association Study
Tumor Marker Prognostic Studies
Statistical Assessment of Medical Papers

Thank you

Associate Editor

MINOR REVISION 10 Jun 2023

Dear EIC,
The great effort in improving the manuscript is highly appreciated. But some sentences were incorrectly added by the authors to the methods section of the abstract. The authors should delete them and add only the study design based on the reviewers' comments.

Editor-in-Chief MINOR REVISION 10 Jun 2023

Dear Author,
Your manuscript still needs revision.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Title: A NATURAL ADDITIVE ALTERNATIVE TO THE COSMETICS INDUSTRY: HAZELNUT AND ITS WASTE PRODUCTS

Id: 137580

Article Type: Research Paper

Dear Editor,

We would like to express our gratification for the opportunity to improve the paper and appreciate your guidance. We have tried our best to ensure the required revising corrections.

We are looking forward to hearing from you at your convenience.

Yours sincerely,

Prof. Dr. Meltem ASAN OZUSAGLAM

RESPONSE TO EDITOR AND REVIEWER

REVIEWER 1

Abstract:

1. Authors should delete Sentences that added after revision. Authors just should mention study design (just few words).

Our response: Thank you so much for your comment. In the method section of the abstract, the sentence that added after revision was deleted. The study design for our study has been added as an experimental study. Changes are marked in red.

Also, because it was the first use of the bacterium in the text, "*L. fermentum* MA-7" was corrected as "*Limosilactobacillus fermentum* MA-7".

Methods: In this experimental study, disc diffusion, minimal inhibition (MIC) and minimal bactericidal (MBC) or fungicidal (MFC) concentrations test were applied to evaluate the antimicrobial potential of the extracts. The sun protection factor (SPF) of the extracts and commercial cream+extract mixtures was determined in vitro. In addition, antimicrobial cream formulations containing hazelnut extracts and *Limosilactobacillus fermentum* MA-7 probiotic candidate lactic acid bacteria from human milk were developed for the pharmaceutical industry to prevent infections, well diffusion test was applied against test microorganisms to evaluate its antimicrobial activity.

3 Revision 2

2 comments · 14 Jun 2023 – 14 Jun 2023

Associate Editor

ACCEPT 14 Jun 2023

Dear EIC,
I reviewed the manuscript again. The great effort in improving the manuscript is highly appreciated.
The authors have addressed all comments.
Thank you

Editor-in-Chief

ACCEPT 14 Jun 2023

Dear Author,
Thank you for paying attention and responding to the reviewer's comments. The manuscript is acceptable now.