

Review of: "Saponins and their synergistic antibacterial activity with traditional antibiotics against *Staphylococcus aureus* and *Escherichia coli*: Review"

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Potential competing interests: No potential competing interests to declare.

The review article is interesting according to synergistic antibacterial activity with traditional antibiotics against *S. aureus* and *E. coli*. The manuscript was written informative. However, there are several major concerns that need to be addressed. As this review article is explaining the antimicrobial action and synergism of saponin it needs to give some explanation of how saponins' effect or blocking bacterial efflux pumps? Besides, possibly saponins can also disrupt the outer membrane of gram-negative bacterial cells, the authors need to review the related literature and add relevant information. It would help the reader if you can add figure or diagram to explain the different mechanisms by which saponins work. The manuscript should provide a thorough discussion regarding the mechanism of action and/or the plausible synergistic effect of the herbal extracts/saponins rich extracts with the antibiotic against certain pathogen species. Additionally, the reference should be double checked and write in consistent form, the article was from the book or from journal should be clear, some volume (number) and pages should be completed as well.

There are some specific comments:

Introduction:

1. The authors told the synergistic antibacterial activity with traditional antibiotics story well, yet a section of the antibiofilm activity of saponins is lacking, as biofilm formation is an important way for bacteria to become tolerant to antibiotics. With respect to biofilm inhibition, the authors should discuss the mechanism of inhibition quorum sensing by saponins.
2. Overview the article, the authors did not take into account the rules of scientific naming of family, genus or species. e.g., states "in families of Agavaceae, Dioscoreaceae, and Liliaceae", the family name should not be italics. Besides, the name of genus and species should follow the name of the authors when mentioned for the first time, the same problem in the Main text section should be modified as well.

Main text:

1. The authors sometimes use "antimicrobial activity of saponins" and sometimes "Antibacterial activity of saponins" to describe their study, what difference they mean? The antimicrobial and antibacterial sections should be combined, since antibacterial are also antimicrobial.

2. Are there certain substances and saponins that produce good bacteriostasis by synergistic action against most bacteria? The information cannot see from the Table 1. Additionally, the references need updating to include more recent ones.
3. What is the obvious difference between steroidal saponins or triterpenoid saponins (mentioned in the article) and the specific mechanism of synergistic action between these two saponins and traditional antibiotics.
4. Figure 1. States "Synergy of plants with antibiotics against bacteria, measured in fractional inhibitory concentration index (FICI)". Is it really plants, or should be saponins as those are the plants products the review is concerned about. Please add some structures of different saponins that have been shown to produce synergism with antibiotics.