



SDI Review Form 1.6

Journal Name:	Microbiology Research Journal International
Manuscript Number:	Ms_MRJI_39218
Title of the Manuscript:	Modeling the variation of inhibition zone diameter in disc diffusion susceptibility test of natural substances and antibiotics
Type of the Article	Original research papers

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
<u>Compulsory</u> REVISION comments	ABSTRACT : - What is the interest of adopting a new measurement unit (ng / mm²), knowing that the current universal unit is simply µg / disk? - Results: We do not see any results. The first sentence is adapted to the methodology, and the second sentence is adapted to the conclusion. Introduction : - The introduction is very long - Lines 26 and 27 "Most of the time, there is no justification on the choice of the concentration tested" : I do not agree. Current recommendations are based on consensus studies. Where it is not tiled, the recommendations recommend the use of dilution (EUCAST, for example) - Lines 27 to 29 "It has also been demonstrated that the compound diffusion creates a gradient of concentration which is one of the reason of the low inhibiting effect at the edges of the inhibiting zone" : The diffusion technique is based on this concentration gradient. If the concentration	ABSTRACT : - The unit µg/disk can not be considered as a perfect unit since disk is not a universal unit of measurement. Moreover, many authors use disk of different diameters and it is important to harmonize Our proposition is for the sake of harmonization and also to have variable values that will balance the regression matrices. - Thanks for the comment, the main objective of our work was to produce a model. So our main result is that model indicated in the first sentence of the results. The second sentence have been modified to be more suitable as proposed by the reviewer. Introduction : - We are not speaking about the dilution methods but of the disk diffusion method. And in this case, many authors reports test with different disk load and even disk diameters. Our observation is based on more than 400 publications; - Thanks very much for the paper suggested, it is very interesting and deals with the correspondence of inhibition diameters and CMI. We agree with what the reviewer says and that lower concentration at the edges can be proportional to the MIC The work also confirm the belt like nature of the concentration gradient around



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	of the antibiotic is monitored on either side of the antibiotic disk, the curve would look like a bell, where the concentration of the antibiotic at the border of the zone of inhibition corresponds to the MIC. Figure 33: http://www.sciencedirect.com/science/article/pii/S2210654515000642 - Lines 34 to 36 “However, it is already an initial solution to the conclusion of King and Dykes [17] who stated that there is no linear or logarithmic relation between inhibition zone size and the concentration of the agent: On the contrary ... http://www.sciencedirect.com/science/article/pii/S2210654515000642 - Lines 44 and 45 “ obtained from hydrodistillation (essential - 45 oil), or by aqueous and ethanol extraction” : It is admitted that the extracts have a complex composition, since they contain very diversified substances. Therefore, it will never be known which substance has antimicrobial activity and at what concentration. In addition, given the pharmacological interactions between the different substances, an extract could have	the disk. However, our work deals with the prediction of the inhibition diameter knowing the compound load on a disk. This citation was added - Regarding line 34-36, the conclusion of Dykes is not contrary to the observations of Jehl 2015 because Dykes and our work deals with the proportionality between the compound concentration and the inhibition diameter in disk diffusion tests. - In our intention, the word substance is a considered as a mixture of compounds. We are aware of the different interaction that compounds in essential oil or extracts can have. We decided to work with the gross substance in order to be more in accordance with the traditional medicine pharmacopoeia. However a sentence has been introduces before the last paragraph of the introduction to clarify this.
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	an antimicrobial effect that results from the synergy between two substances that would not have their own antibacterial effect. On the contrary, antagonism between two active substances could nullify the effect of both and mask true antimicrobial activity. The reason for this is to separate the substances from the same extract, to purify them and to provide proof that they are pure before evaluating their respective antimicrobial activities. MATERIAL AND METHODS - Line 101 “antimicrobial agent concentration” : Inconnue pour les extraits RESULTS AND DISCUSSION - Table 2 “AMO_BC” : Bacillus cereus is naturally resistant to aminopenicillins, including amoxicillin. There should be no zone of inhibition. - Table 2 “ AMP_Shi / 26,26 and 25,6 “ : Is it correct ?	MATERIAL AND METHODS - “agent” is a common name we used because antibiotics, essential oil and extracts were tested in this work. For homogeneity, the term antimicrobial substance was used to replace agent as in the rest of the work. RESULTS AND DISCUSSION - The reviewer can not be so categorical with species reaction to antibiotics. It depends on many factors and antibiotic resistance is rarely a specie natural trait but a strain related property. We have proposed other literature data in accordance with our results: Liyanage et al (2016), Evolution of amoxicillin and sulphonamide removal by Bacillus cereus, enterobacter ludwigii and enterobacter sp., environmental and natural resources J., 14(1):39-4339, and Tumbull et al. J Clin Microbiol. 2004 Aug; 42(8): 3626–3634. - Thanks for calling for our attention. In fact there was a typing mistake 25.6 is in reality 23.6. this Information on Table 2 is corrected.
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<u>Minor</u> REVISION comments	ABSTRACT : - Replace “microbial sensitivity test” by “Antimicrobial susceptibility testing” - Specify the duration of the study, 5 or 6 months? - “Data was divided into two groups and one used together with literature data available for validation” : Ambiguous sentence - Conclusion : Return to the line Introduction : - Line 20 : Specify that MIC is Minimum inhibitory concentration - Lines 20 to 24 : After the reminders on diffusion and dilution, a bioautography reminder is expected. - Line 37 “There are many reasons” : It is desirable to specify them all	ABSTRACT : - Replacement of antimicrobial susceptibility testing done - Duration of the study: 6 months, added in the text - Sentence corrected as “Data was divided into two groups and one used for validation together with available literature data”. - Conclusion return to the line done. Introduction : - Specification of the term MIC (Minimum Inhibitory Concentration). - Thanks, the sentence was modified and now reads.
<u>Optional/General</u> comments		