



SDI Review Form 1.6

Journal Name:	Journal of Advances in Medical and Pharmaceutical Sciences
Manuscript Number:	Ms_JAMPS_48110
Title of the Manuscript:	SIMULTANEOUS QUANTIFICATION OF ACETAMINOPHEN-(PARACETAMOL), CAFFEINE AND, IBUPROFEN IN FIXED DOSE COMBINATION DRUG USING HPLC WITH UV DETECTION
Type of the Article	Original Research Article

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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)
Compulsory REVISION comments	<p>Development a simple, fast and effective method for the active compounds assay in a multicomponent drug is very important problem in pharmaceutical analysis. Authors proposed the HPLC method for this purposes and presented some materials about development and validation of the proposed method.</p>	Authors do agree.
Minor REVISION comments	<p>1. In the introduction part authors discussed about titrimetric and UV-spectroscopy methods for the paracetamol, caffeine and ibuprofen method determination, and did not mentioned about HPLC methods, which was printed in the different scientific journals. For example, J Sep Sci. 2015 May;38(10):1657-62. doi: 10.1002/jssc.201401387.; Anal Chem Ind J. 2017;17(1):116.; Am. J. PharmTech Res. 2015; 5(5) 349, etc. Why the proposed method is better than existed ones? Why is necessary to develop one more HPLC method for this purposes? This is should be clear presented</p> <p>2. The presented chromatogram are awful. I practically cannot see chromatographic peaks. Should be corrected and clear presented.</p> <p>3. As can "see" from the presented chromatograms the tailing factor of the investigated components are more than 2, which is not accessible for the chromatographic assay method (0.9-1.5 is preferably). Why authors did not discussed about tailing? And may be better to use more acidified mobile phase (pH 2.5, for example) for the correction of this problem?</p> <p>4. Parameters of the linear equation should be better presented in table and as $Y=(A \pm Sa) + (B \pm Sb) \cdot X$. And in the same table presented LOQ and LOD data.</p> <p>5. Part 3.1.2.1 Residual plots. What is the criterion of acceptability of the residuals (error), which was calculated by authors? Requirements are good or not for the assay method?</p> <p>6. Part 3.1.3. The placebo chromatogram is necessary to present, that authors can made a conclusion that "The chromatograms obtained with the mixture showed no interfering peaks in the same retention time for the Acetaminophen, Caffeine and Ibuprofen, indicating that, other compounds such as the excipients do not co-elute with the main peaks"</p> <p>7. Maxigesic tablets should be excluded from this manuscript so did not content caffeine as active compound.</p>	<p>1. Quite agree with reviewer. The existence of such methods has been duly mentioned in the revised manuscript. However, the proposed method is better because it assembles simple analytical instruments and makes use of cost effective solvents (for example the case of Acetonitrile and Methanol) to achieve a reliable results in the shortest possible time. Also, no economically minded pharmaceutical manufacturing company will be delighted in using a high volume of phosphate solution in a C18 chromatographic column- as the other HPLC methods propose, because phosphate solutions wear columns quickly. Hence, this proposed method ensconces pharmaceutical manufacturing companies, especially in developing countries.</p> <p>2. Agree with reviewer. Chromatograms have now been clearly presented.</p> <p>3. Chromatograms are clearly presented now. By using the formula $T_s = W_{0.05}/2f$, the Tailing factor (T_t) of each of the components of interest was approximately 1 and not 2. A pH of 2.5 was tested, chromatograms were almost eluting together, and hence pH 3.2 was better. Tailing was briefly discussed in table 1, in addition to other system suitability parameters including the efficiency of the column.</p> <p>4. Agree with reviewer. Correction effected.</p> <p>5. Statistically, residual plots are used to check linear relationship within a data. Residual plots must be normally distributed around the point zero on the vertical axis. Hence the residual plot was to prove the linearity of the developed method, as can be seen that, the residuals are normally distributed. That is good for the developed method.</p> <p>6. Strongly Agree with reviewer. Chromatogram of Placebo has been presented in the manuscript now.</p> <p>7. In the introduction, it was clearly stated that the developed analytical method, though, specifically for formulations of Paracetamol/Caffeine/Ibuprofen combination products, it can also be used to assay combination products of Paracetamol and Ibuprofen without Caffeine</p>



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	8. Authors cited and used data from USP 29. Why? The actual of USP pharmacopoeia is USP41	as an adjuvant, including raw materials of Acetaminophen, Caffeine and Ibuprofen. Thus the method was used to analyse Maxigesic tablets, hence its relevance in the manuscript. 8. Authors do agree with the reviewer, and have accordingly deleted this reference.
Optional/General comments	The manuscript required grammatical correction: a lot of misprints and mistakes	A lot of the misprints have been corrected. If there are grammatical errors Authors would be glad to receive notification for immediate correction.

PART 2:

	Reviewer's comment	Author's comment <i>(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)</i>
Are there ethical issues in this manuscript?	<i>(If yes, Kindly please write down the ethical issues here in details)</i>	There are no competing interest as far as this manuscript is concerned.