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Journal Name:	Journal of Advances in Medical and Pharmaceutical Sciences
Manuscript Number:	2015_JAMPS_16507
Title of the Manuscript:	Evaluation of the Physicochemical Properties and Quality Indices of Six Brands of Tadalafil Drug Products Marketed in Nigeria
Type of the Article	Review Article

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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.

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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	1) Authors should really revised the abstract, especially the structure of the abstract. Now, it is mostly like the summarization of the results. 2) Did you carry out all the experiments under the regulatory of the Pharmacopoeia documentation, especially the dissolution tests to comparable with their results? If yes, it should be clearly specified, at least, in the part of methodology and the reference to the literature has to be included. Different conditions of the test really change the dissolution profiles a lot. Did you add any type of surfactant to your dissolution medium? What about other type of dissolution medium with different pH? We have	The abstract has been revised 1. The experiments were done using, where applicable, pharmacopoeia/official methods. Other methods employed especially for dissolution tests were validated methods and referenced please see ref no 9, 11 and 24). The dissolution performed here was without a surfactant. Inclusion of surfactant will mimic the absorptive media (in vivo) i.e. more relevant media. This was however not our design. We have followed previous and established methods where sample are withdrawn and fresh media replaced within the available resources. 3. There are several parameters deducible from dissolution studies. The C₄₅ and T₉₀ are British Pharmacopoeia parameters that is acceptable. The parameters used



SDI Review Form 1.6

	experience with the pharmacopoeial phosphate buffer with addition of SDS for tadalafil. Modern dissolution tests are carried out: The sampling during the dissolution tests is made continuously due to flow sampling cell (A spectral equipment is connected to the dissolution apparatus) and there is no replacing with the fresh dissolution medium as you described in section 2.2.8. Did you carried out it with the agreement of pharmacopoeia? 3) Why you compared the products with the parameters C45 and T70? Generally, the Cmax and Tmax parameters are used for it. Anyway, all the used parameters (included also DE and PAE) must be described in the part of methodology. 4) Keep in mind that much more important are the results of BE	
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SDI Review Form 1.6

	study (made <i>in vivo</i> on humans; concentration of the drug in their blood is monitored over time) than the dissolution tests (made <i>in vitro</i> in dissolution testers; concentration of the drug in the dissolution liquid is monitored over time). Once any two drugs have been stated bioequivalent by the regulatory agency, it cannot be claimed that they are not bioequivalent based only on a dissolution test. You would have made a new BE study to confirm your statement. So even if the quality (in the context of the behaviour of the dosage form in the human body) was different in the dissolution test, in the human body they would behave bioequivalent. 5) It is well known that the higher price of the originator's product is in relationship with the price spent on the research of the new	4. The scope of this research did not include bioequivalency. The pharmaceutical equivalence was targeted as a preliminary study. We have not claimed any form of inequivalency <i>in vivo</i>, by our results. It is however unlikely that products with different physicochemical outcomes, including chemical content (assay) differences will eventually turn out to be bioequivalent. A further study <i>in vivo</i> may prove this to be right or wrong. 5. Yes, the cost of research is enormous. The discoverer of a new molecule is granted a sole right of sale of the molecule for about 5-10 years, for the cost of the research to be gained after this time, the higher cost than other brands must be justified by proven excellence of physicochemical and <i>in vivo</i> outcomes compared to other generic product.
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SDI Review Form 1.6

	product. The generic manufacturers did not spend so much money during the development of his generic product. For that reason, there is no reason why to justify the different prices of the innovator and brand products based on the results presented. 6) Revise the sentence at line n.152-153. The main result of your investigation really is that all tested products are officially registered with NAFDAC??? 7) The description of the methodology needs a revision. It would be nearly impossible to reproduce the experiment under the current description.	ology herein is as as possible. Anyone who follow up on this work line by line and may compare the results with here. Further clarification has to be calibration details
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SDI Review Form 1.6

Minor REVISION comments	1) In the methodology section 2.1.2. Apparatus employed in the study, there is a strange usage of the brackets. Please revise this section. 3) Section 2.2.1 Visual inspection of drug products. Even the size was not measured with any calliper? 4) Section 2.2.2 Tablet weight uniformity test. What analytical balances was used? Define the accuracy of the balances, number of decimal digits allowed by the balances at least. 5) Section 2.2.3 Hardness test. What tester did you use? Please revise the word "subjecting" in the first sentence of this section. Maybe the fault is on my side, but I cannot understand meaning of this word how it is used. 6) Section 2.2.4 Friability test. Please, fill the name and country of the manufacturer of the friabilator. Do the same for all equipment mentioned	The section has been revised. Brackets removed. The size of the tablets or capsules of the sampled brands was not part of the design. The definition requested here was not included in the entry. The analytical bal was specified in section 2.1.2. It measures accurately to 2 dec. places. 5. Tester specified in section 2.1.2 'subjecting' removed and sentence retested. 6. This is also in section 2.1.2 7. We think the sections can be separated for clarity. 8. 'About' is removed/deleted. The HPLC system is already in 2.1.2 9. USP 10. The full names of the statistical tests included
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SDI Review Form 1.6

	in this manuscript, section 2.2.5. as well. E.g. was tested with "the full name of the equipment" ("Manufacturer", "Country"). 7) Section 2.2.6 should be inserted to the section 2.2.7. 8) Section 2.2.7. I really do not like "about 80 ml". It was not exactly 80 ml of methanol? The description of the equipment is again missing. 9) Section 2.2.8. Describe the used apparatus. Did you use vessels or different pharmacopoeial stirring apparatus? 10) Section 2.2.9. The used statistical methods are well known. But I would recommend to add full names of these tests. 11) How you did the measurement of the melting point and chemical content? Methodology, especially the equipment, should be described. 12) How did you make the calibration curve? Describe 13) Why is included Fig.2 of the chromatogram?	11. The chemical content was determined using HPLC system and details already described and equipment in 2.1.2 12 The detail of the calibration is inserted in section 2.2.7 13. The chromatogram is deleted (Fig 2) 4. Powders were made into capsules. This has been reflected in section 2.2.7 15 The correction has been reflected to 15.20 16 Other reasons have been reflected in the revision. 17 When tablet products are properly formulated (ie using the right excipients and quantity), the crushing strengths may be satisfactory. The type of packaging may affect the crushing strength especially if moisture is absorbed along the shelf life. Better packaging excludes moisture and any possible interaction with excipient (eg, starch). This area has been recasted for clarity. 18 The appropriate table is Table 2 and is reflected in line 141 and line 147 is reflected Table 3 19 The format is revised for uniformity as At and 2,000.00
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	There is no comparison with other chromatograms and no description of the mentioned one either. 14) Some of measured products were capsules. Was powder or pellets inside the capsules? 15) Line n. 130. ...deviation over 16%. I cannot see any value over 16% in Table 2. 16) Lines n. 132. Are not there other reasons why the weight uniformity was observed out the range for some products than only the poor flow of the granules? 17) Lines n. 138-139. The sentence: However, this may ... since they were all blister packed. How does the blister packing relate with crushing strength of the tablet? Please answer this question. 18) Line 141 and 147. Incorrect cross reference to Table 3. There is Table 2 mentioned. 19) Somewhere you gave the process with crossed N and somewhere did not; and the value of the price in the format "N 2 000" and	
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	somewhere like "N2,000.00". Be consisted in the formats. Please revise. 20) What is the NAFDAC, written in line 153? 21) Table 2. Zero friability of some products is more than strange. What if you write more decimal digits? Is there any friability seen then?	
<u>Optional/General</u> comments		