PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Beliefs, Practices and Knowledge of Community Pharmacists Regarding Complementary and Alternative Medicine: National Cross-Sectional Study in Lebanon
AUTHORS	Alameddine, Mohamad; Hijazi, Mohamad Ali; Shatila, Hibeh; El-Lakany, Abdalla; Aboul Ela, Maha; Kharroubi, Samer; Naja, Farah

VERSION 1 - REVIEW

REVIEWER	Carolina Oi Lam Ung Institute of Chinese Medical Sciences, University of Macau, China
REVIEW RETURNED	17-Jul-2018

GENERAL COMMENTS	Dear authors, I appreciate the opportunity to review your manuscript and find your research question highly relevant to addressing the consumers' needs, as well as the development of pharmacist profession. In many countries, the use of traditional/complementary medicines is mainly consumer driven and pharmacists are well positioned to provide support and reliable information to consumers to help them make informed decision. Your research reports the current situation in Lebanon and contributes to enhancing the global perspective on this research topic. Having said that, there are some fundamental issues requiring clarification: 1. The terms "complementary and alternative medicine (CAM)", "CAM products" and "CAM practices" were used in the manuscript. Please define each of these terms according to the national situation/regulation in Lebanon. 2. Please provide an overview of the regulation of pharmacy and pharmacist in Lebanon in order to facilitate the understanding of the study design and findings. 3. Regarding Methods, please explain the following: 3.1 How pharmacies were selected in each stratum in order to cover as much diversity as possible within one geographic location. 3.2 How was the questionnaire design informed? 3.3 The relevance of the question "How long has this pharmacy been opened for?" in Table 2. 3.4 CAM and CAM products are different but it seems that these terms were used interchangeably in Table 3. Please confirm. 3.5 What does traditional prescription therapy in "The use of CAM products should not be limited to patients who have failed traditional prescription therapy" from Table 3 refer to?

	3.6 It appears that CAM products and commercially marketed CAM products in Table 3 refer to different scope of products. Please clarify. Also, please confirm if the participants were aware of the difference. 3.7 What does “Media plays a positive role in educating patents about CAM” in Table 3 mean? Why “patients” is used but not “consumers”? 3.8 What does “natural practitioners” in Table 4a refer to? 3.9 Why were the ingredients mentioned in Table 5 selected? How were they relevant to CAM products in Lebanon? 3.10 What are the correct answers for the statements in Table 5. Please also support with evidence based information. 3.11 Were the participants given opportunities to provide qualitative information in the questionnaire? 4. Regarding findings, please explain the following: 4.1 The number of responses to the majority of the questions is not 357 and slight variations exist from question to question. Recommend to include only completed questionnaire in the findings, or specify clearly the number of responses for each question and justify the missing responses. 4.2 Please explain the findings that “no pharmacist worked in some of the pharmacies” as shown in Table 2. 4.3 As shown in Table 4a, 149 participants had experience of “reporting toxic or undesirable effect occurred with patients using CAM products”. In Table 4b, only 69 responses were reported. Please explain. 4.4 Recommend to conduct further data analysis to supplement the descriptive findings. 5. Regarding Discussion, please explain the following: 5.1 Please provide citation to support important arguments. E.g. “MENA region hosting one of the fastest growing markets of CAM products”, “High frequency of pharmacies reporting the selling of such products”, “This is despite pharmacists being well knowledgeable of the purpose of CAM use.”, “One explanation for this is the means through…..the promotion of their products.” 5.2 What is the difference in the functions of OPL and MoPH? 5.3 Considering the suggestion of “learn from the experience of the US”, how do the authors find the strengths as well as the limitations of the current regulatory system of dietary supplements in the US? How do dietary supplements in the US relate to CAM products in Lebanon? 6. Proof reading of the manuscript by a native English speaker is recommended. I hope you find the comments useful and relevant to improving your manuscript.

REVIEWER	Naser Shraim An-Najah National University, Palestine
REVIEW RETURNED	17-Jul-2018

GENERAL COMMENTS	Overall, this manuscript covers an important topic and is relevant to health outcomes of patients. However, my comments are

	intended to help strengthen the paper for publication. I hope you find them helpful. Abstract: Design, methods and setting need to be more fully elucidated. Alternatively, don't mention any figures in the methods and include this data in the results section. Results It would be more helpful to provide a response rate of the participants that who completed the questionnaire Main manuscript: Methods: 1. I d o believe that attitudes about CAM were not measured in this study, but beliefs (one component of attitudes) were measured. Please correct all references to attitude about CAM and change to beliefs about CAM to accurately reflect what was measured. 2. Could you please give more details about the data collection form particularly in section 2, 3 and 4. Did you develop the 'knowledge-based' questions based on what you would expect pharmacists to know (so were these questions about CAM that is commonly purchased in a community pharmacy or about CAM that is associated with numerous safety concerns/interactions etc.). What are the types of questions used? And what are the options given to participants to choose? What resources did you use to ascertain the correct answer to the questions? It would be useful if Table 5 was clear about the pharmacists' answers versus the correct answers 3. what is the reliability and validity of this scale 4. Your study only measured knowledge about herbals and supplementary products (not different types and modalities of CAM in general) which is similar to the gap in the literature that was identified also in introduction. Please clarify. 5. I do ask authors to score the knowledge as a 10-item scale and then assess the association of knowledge score among the socio-demographic categories of participants. 6. Recruitment/response rates: it could be clearer as to how the pharmacists were invited/recruited to participate in the study, what you did to maximize the response rate, did the participant completed the questionnaire in the presence of researcher and how long would participant take to complete the questionnaire? The setting of the study was community pharmacies what about different pharmacy location as hospital pharmacists therefore the title of the manuscript should include community "… community pharmacists….." 7. Statistical analysis: Descriptive statistics is insufficient for this kind of studies you need to score the knowledge and or beliefs and to compare the median scores as appropriate Discussion: 8. When comparing findings on knowledge, it is not clear how similar/different your knowledge measure was with other published findings. Please clarify. 9. Please refer to literature and find similar studies conducted nearby in the region as Palestine, Jordan, Qatar and Iran also away in the US, Australia Singapore and then compare your findings with those relevant studies 10. Throughout the paper, you switch back and forth between CAM and herbals (one CAM modality). In addition, you only measured herbal knowledge and not CAM knowledge; therefore, some discussion points may be misleading/confusing. Much of your discussion focuses on herbal findings (including the

	knowledge measure) and should be situated in that context. Please be clear throughout Minor Typos: Throughout the manuscript you should be consistent for example Health care or healthcare or health-care Table 1: Title pharmacists should be replaced by pharmacies

REVIEWER	Peter Bai James University of Technology Sydney, Sydney Australia
REVIEW RETURNED	17-Jul-2018

GENERAL COMMENTS	The authors have presented interesting findings on knowledge attitude and practice of pharmacists toward CAM in Lebanon. However, there key issues that need to be addressed INTRODUCTION 1.Paragraph 1 line 16: According to the World Health Organization (WHO), in developing countries, 65-80% of the population depends essentially on plants for primary health care.3, Please provide the scientific basis for this statement that is based on a recent original research or systematic review of the available literature or report. The current reference is not appropriate Methods 1. With regards to the questionnaire, what informed its design in the first place and what also informed the inclusion of the question of how long the pharmacy opens? 2. I have some issues with the inclusion of pilot data into the main study data based on the fact that no changes were made to survey tool. The essence of piloting a study is not just to see if the survey tool is adaptive to the local setting. Piloting a study assesses the 1.the process of conducting the study with regards recruitment, non-response. It looks at whether the inclusion criteria is sufficient or too restrictive 2. it also assesses the time and resource problems as well as(3) data management issues. All these issues in addition to others logistical issues can influence the nature of the pilot data collected and eventually the main study. Except the authors are stating categorically that no changes were made with regards every aspect of the pilot study including ones not normally reported in research papers, then their claim can stand. As researchers, we know that there are scientific and logistical challenges that come to light when piloting a study which informs the way process in which the main study is done and as such informs the nature of the data collected. As such the way and manner in which the final study would have been conducted would be different compared the to the pilot study and that has the tendency to influence the data collected, results got after data analysis and conclusion made based on those findings. Another issue is that , the non-probability sample method was used to collect data from the 16 pharmacists for the pilot study whereas the in the main study probability sample method was used. It is difficult to understand how data collected from different sampling methods can be used together in the final analysis. 3. Authors need to elaborate on how outcome variables were measured and what statistical tests were used to analyze the data

	Results 1.I see only descriptive statistics were done. It would have been good to see some inferential statistical analysis done. e.g one might want to know how CAM knowledge among pharmacist is influenced by their socio-demographic characteristics like age, qualification, level of experience, prior knowledge about CAM etc. As it stands now what is presented is good but not enough. some inferential statistics should be done. Discussion 1. The study reports that pharmacist in Lebanon often provides advice on the safe use of CAM products but their knowledge on the safety of CAM product is limited. It begs the question as to what type of advice is given and how that influenced patient health outcome. It will be good if the implications of the above anomaly are discussed. Please see the attached reviewed manuscript for other comments

VERSION 1 – AUTHOR RESPONSE

Reviewer #1. Professor Carolina Oi Lam Ung

(1) The terms “complementary and alternative medicine (CAM)”, “CAM products” and “CAM practices” were used in the manuscript. Please define each of these terms according to the national situation/regulation in Lebanon.

• Author’s response: As per the reviewer recommendation, the definition of ‘CAM products’ was added to the Introduction section of the revised manuscript, as follows ‘The United States (US) National Center for Complementary and Integrative Health (NCCIH) divides CAM into two main categories: (1) natural CAM products, such as herbs, vitamins and minerals and probiotics; and (2) mind and body therapies, most common of which are yoga, chiropractic and osteopathic manipulation, meditation, and massage therapy2.’ (Page 4, lines 6-11).

CAM-related practices among pharmacists were specified I the revised manuscript as selling CAM, advising patient on the safe use of CAM, reporting of CAM toxic effects and checking for CAM-drug interactions. (Page 7, lines 24-26)

(2) Please provide an overview of the regulation of pharmacy and pharmacist in Lebanon in order to facilitate the understanding of the study design and findings.

• Author’s response: We are delighted to provide information on the regulation of pharmacists and pharmacies in Lebanon, as follows ‘In the country, the Ministry of Public Health (MoPH) regulates the profession of pharmacy, through granting the 1) license to practice for pharmacists and 2) license to open a pharmacy. For the latter, the pharmacist ought to be registered within the Order of Pharmacists in Lebanon (OPL).33 (Page 5, lines 22-26).

(3) Methods:

3.1 How pharmacies were selected in each stratum in order to cover as much diversity as possible within one geographic location.

• Author's response: Within each stratum (governorate), pharmacies were selected at random from the list of all pharmacies within this stratum. The text of the manuscript was revised to clearly reflect the selection of pharmacies within each stratum. (Page 6, lines 7-8).

3.2 How was the questionnaire design informed?

• Author's response: The design of the questionnaire used in the data collection for this study was informed by a thorough review of relevant past literature and by careful examination of the local context (References number 16, 23, 24, 34). The Methods section was revised accordingly. (Page 7, lines 1-3).

3.3 The relevance of the question "How long has this pharmacy been opened for? in Table 2

• Author's response: The following text was added to the Methods section to explain the relevance of the question 'how long was the pharmacy open for': The latter question was included because in the local context, the longer the duration the pharmacy has been opened for, the more likely its clientele would develop a personalised relationship with the pharmacist allowing for a better communication of their health needs and concerns. (Page 7, lines 16-19).

3.4 CAM and CAM products are different but it seems that these terms were used interchangeably in Table 3. Please confirm.

• Author's response: We thank the reviewer for highlighting this issue. For clarification, the following revisions were undertaken: 1) A statement was added at the beginning of the manuscript 'In this manuscript, CAM refers to natural CAM products' (Page 4, lines 10-11); 2) in table 3, 'CAM products' was used instead of 'CAM'.

3.5 What does traditional prescription therapy in "The use of CAM products should not be limited to patients who have failed traditional prescription therapy" from Table 3 refer to?

• Author's response: We apologize for this confusion. In this question 'Traditional prescription therapy' refer to 'conventional medicine therapy'. Accordingly, the questions was reworded as follows 'The use of CAM products should not be limited to patients who have failed conventional medicine therapy'.

3.6 It appears that CAM products and commercially marketed CAM products in Table 3 refer to different scope of products. Please clarify. Also, please confirm if the participants were aware of the difference.

• Author's response: We thank the reviewer for highlighting this discrepancy. In fact, commercially marketed CAM products refer to CAM products available in the Lebanese market. Participants were made aware that questions in this section are specific to the CAM products available in the Lebanese market. The text in the Methods (page 7, line 21) as well as table 3 was rephrased to clearly reflect the meaning of the questions.

3.7 What does "Media plays a positive role in educating patents about CAM" in Table 3 mean? Why "patients" is used but not "consumers"?

• Author's response: This question was revised in the manuscript and the word 'patients' was replaced by 'consumers'. This question meant to investigate the beliefs of pharmacists towards the role of media in educating consumers about the safe use of CAM products. In this question media referred to all kinds of broadcasting and narrowcasting medium such as newspapers, magazines, TV, radio, billboards, direct mail, telephone, fax, and internet. The text of the methods (page 7, line 22) and table 3 were revised for clarity.

3.8 What does "natural practitioners" in Table 4a refer to?

• Author's response: For clarity, 'natural practitioner' was replaced by 'naturopath'. The latter is a health practitioner who uses natural therapies, including herbal and nutritional supplements (CAM products).

3.9 Why were the ingredients mentioned in Table 5 selected? How were they relevant to CAM products in Lebanon?

• Author's response: The text of the manuscript was revised to include a justification for the choice of questions in table 5, as follows: The last section of the questionnaire addressed the pharmacist's knowledge about CAM products. A total of ten questions were selected to address the uses, side effects and drug interactions of commonly sold CAM products in the Lebanese market. According to a previous investigation by the authors, vitamin C was the most commonly sold CAM product (25%), followed by ginseng (22%), vitamin B (13%), Gingko (14%), Omega 3 fatty acids (9.5%), Echinacea (9.5%) and Valerian (7.4%) (unpublished data). The formulation of the questions around these products was carried out by an expert panel of pharmacists including MH, ME (authors), and Dr Ghassan Al Amine (previous president of the OPL), and in consultation with relevant literature.23,35. (Page 7, 28-34 and page 8, lines 1-3).

3.10 What are the correct answers for the statements in Table 5. Please also support with evidence based information.

• Author's response: As requested by the reviewer, a column was added to table 5 indicating the correct answers. Each answer was supported by relevant literature.

3.11 Were the participants given opportunities to provide qualitative information in the questionnaire?

• Author's response: This study was planned as a quantitative assessment of pharmacists', beliefs, practices and knowledge with regards to CAM, using a structured questionnaire. That said, we agree with the reviewer that future studies aiming to qualitatively examine these parameters among pharmacists could complement the results of the quantitative investigations and provide a more complete evaluation of the subject matter. The Limitation section of the manuscript was revised accordingly and the following text was added 'It is important to note that this study relied mainly on quantitative assessment. Future studies aiming to qualitatively examine pharmacists' beliefs, practices and knowledge with regards to CAM could complement the results of quantitative investigations and provide a more complete evaluation of the subject matter' (Page 14, lines 24-28).

(4) Results

4.1 The number of responses to the majority of the questions is not 357 and slight variations exist from question to question. Recommend to include only completed questionnaire in the findings, or specify clearly the number of responses for each question and justify the missing responses.

• Author's response: A comment of reviewer 2 recommended the removal of questionnaires collected during the pilot phase (n=16). The sample size was therefore reduced to 341. As recommended by this reviewer, only complete questionnaires (with no missing data) were included in the analysis, hence 31 questionnaires were also removed, reducing the sample size to 310. The following sentence was added to the revised Results section of the manuscript 'Of the 341 questionnaires, only those with complete data were included in this study (n=310).' (Page 8, lines 27-28).

4.2 Please explain the findings that "no pharmacist worked in some of the pharmacies" as shown in Table 2.

• Author's response: We apologize for this ambiguity. The text was revised to clarify that the question inquired about 'How many pharmacists work in this pharmacy, in addition to yourself?'

4.3 As shown in Table 4a, 149 participants had experience of “reporting toxic or undesirable effect occurred with patients using CAM products”. In Table 4b, only 69 responses were reported. Please explain.

• Author’s response: It is possible that participants were hesitant to answer this question because they were not sure of the correct answer. A sentence was added to the Discussion section to explain this discrepancy, as follows ‘Within this context it is important to note that, out of 123 pharmacists who had experience with reporting toxic or undesirable effects, only 58 indicated to whom they report such effects (47.2%). It is possible that participants were hesitant to answer this question because they were not sure of the correct answer. This further highlights the need to regulate the reporting of toxic effects and to clearly inform the pharmacists of the existing reporting channels.’ (Page 12, lines 31-34 and page 13, lines 1-2). Please note that the numbers in the revised manuscript have changed given the revisions in the sample size (exclusion of participants with incomplete data and those collected during the pilot phase).

4.4 Recommend to conduct further data analysis to supplement the descriptive findings.

• Author’s response: This comment was also raised by the two other reviewers of this manuscript, and was answered as follows: ‘According to reviewers comment, additional data analyses were conducted to supplement the descriptive findings. More specifically, the knowledge questions were scored as 10-item scale and the associations of this knowledge score among the socio-demographic categories of participants were evaluated using simple and multiple linear regression. The text of the various sections of the manuscript was revised to reflect the additional analyses’.

(5) Discussion

5.1 Please provide citation to support important arguments. E.g. “MENA region hosting one of the fastest growing markets of CAM products”, “High frequency of pharmacies reporting the selling of such products”, “This is despite pharmacists being well knowledgeable of the purpose of CAM use.”, “One explanation for this is the means through…..the promotion of their products.”

• Author’s response: We thank the reviewer for her suggestions, accordingly:

o We have revised the argument as such ‘The Middle East and North Africa Region (MENA) hosts a growing market of CAM products’ and the following reference was added : Gruenwald J, Herzberg F: The Global Nutraceuticals Market. Business Briefing: Innovative Food Ingredients 2002, 28-31.

o “High frequency of pharmacies reporting the selling of such products”- This argument is stemming from our findings where only 3.9% of pharmacists indicated not selling CAM products in their pharmacies. The text has been clarified in this regards.

o “This is despite pharmacists being well knowledgeable of the purpose of CAM use.” – In light of other comments of the reviewers, this argument was deleted from the revised manuscript.

o “One explanation for this is the means through…..the promotion of their products.”- We have modified the statement to read ‘One possible explanation …. promotion of their products’ and added supportive references for this statement.

5.2 What is the difference in the functions of OPL and MoPH?

• Author’s response: The Ministry of Health is responsible for the general regulation of pharmaceutical and CAM products in Lebanon. It has the ultimate responsibility for ensuring public wellbeing and safety. For example, the MoPH is responsible for the: drug laws and regulations, drug registration, quality assurance of pharmaceutical products, Lebanese national drug database, drugs public price list, drug recalls, national OTC medicine list, as well as the list of essential medicines. The

Ministry also issues certificates related to pharmacies and pharmacists' practice and carries out regular inspection of pharmacies and drug stores.

The Order of Pharmacists in Lebanon (OPL), on the other hand, is an independent not for profit entity which seeks to raise the level of the profession, strive to enforce laws, defend the rights of pharmacists, improve the level of their practice and develop their scientific competencies. The OPL is responsible for preserving the rights and interests of pharmacists and for supervising their moral duties and dignities issuing disciplinary actions if necessary.

The OPL plays an important consultative and lobbying role vis-à-vis the MoPH and the government. OPL Offers opinion on drafted laws and lobbies for matters that affect the rights and professional status of pharmacists.

5.3 Considering the suggestion of "learn from the experience of the US", how do the authors find the strengths as well as the limitations of the current regulatory system of dietary supplements in the US? How do dietary supplements in the US relate to CAM products in Lebanon?

• Author's response: There are some commonalities between the range of dietary supplements and CAM products offered in Lebanon and the US. In fact, many of the products manufactured and/or sold in the US are also sold in Lebanon. Having said that, the US market is obviously much larger and more diverse than that of Lebanon. From a regulatory point of view, there is no counterpart for the US FDA in Lebanon. The MoPH has had some initiatives to protect consumers' health but more efforts are needed to ensure public safety. This is why the authors felt that Lebanon could learn from the experience of FDA, among other similar agencies in the world.

6. Proof reading of the manuscript by a native English speaker is recommended.

• Author's response: We thank the reviewer for this suggestion, we have thoroughly reviewed the manuscript to ensure the absence of editorial or grammatical errors. We sincerely hope the edits would enhance readability and addresses any concerns with language.

Reviewer #2. Professor Naser Shraim

(1) Abstract

1.1 Design, methods and setting need to be more fully elucidated. Alternatively, don't mention any figures in the methods and include this data in the results section.

• Author's response: The sections of the Abstract were revised as per the reviewer's recommendation.

1.2 Results It would be more helpful to provide a response rate of the participants that who completed the questionnaire

• Author's response: As suggested by the reviewer, the following sentence was added at the beginning of the Results section in the abstract: 'A total of 341 pharmacists agreed to participate (response rate: 86%). Pharmacists with complete data were included in this study (n=310)'.

(2) Methods:

2.1 I d o believe that attitudes about CAM were not measured in this study, but beliefs (one component of attitudes) were measured. Please correct all references to attitude about CAM and change to beliefs about CAM to accurately reflect what was measured.

• Author's response: We thank the reviewer for this comment. Accordingly the text of the manuscript (including title and abstract) was revised to replace 'attitudes' by 'beliefs'.

2.2 Could you please give more details about the data collection form particularly in section 2, 3 and 4: Did you develop the 'knowledge-based' questions based on what you would expect pharmacists to know (so were these questions about CAM that is commonly purchased in a community pharmacy or about CAM that is associated with numerous safety concerns/interactions etc.). What are the types of questions used? And what are the options given to participants to choose? What resources did you use to ascertain the correct answer to the questions? It would be useful if Table 5 was clear about the pharmacists' answers versus the correct answers

• Author's response: As recommended by the reviewer, further details were added to the Methods of development of sections 2, 3, and 4 of the questionnaire. With regards to section 4, the following text as added: 'The last section of the questionnaire addressed the pharmacist's knowledge about CAM products, covering the uses, side effect, and interactions of commonly sold CAM products in Lebanon. A total of ten questions were selected to address the uses, side effects and drug interactions of commonly sold CAM products in the Lebanese market. According to a previous investigation by the authors, vitamin C was the most commonly sold CAM product (25%), followed by ginseng (22%), vitamin B (13%), Gingko (14%), Omega 3 fatty acids (9.5%), Echinacea (9.5%) and Valerian (7.4%) (unpublished data). The formulation of the questions around these products was carried out by an expert panel of pharmacists including MH, ME (authors), and Dr Ghassan Al Amine previous president of the OPL), and in consultation with relevant literature.23,35.' (Page 7, lines 28-34 and page 8, lines 1-3). In addition, in table 5, the correct answer with supporting evidence was added.

2.3 what is the reliability and validity of this scale

• Author's response: Although a few questionnaires were validated to assess the CAM-related beliefs, practices and knowledge among specific population, such as nurses, and medical students46,47, none was available for use among pharmacists. Therefore, in this study, the questionnaire was rather based on expert opinion whereby its content was validated by a panel consisting of a pharmacist, nutrition epidemiologist, biostatistician and a health policy expert. The Limitation section of the manuscript was revised to indicate that future studies are needed to examine the validity and reliability of questionnaires assessing CAM-related beliefs, practices and knowledge among pharmacists. (Page 14, lines 23-28).

2.4 Your study only measured knowledge about herbals and supplementary products (not different types and modalities of CAM in general) which is similar to the gap in the literature that was identified also in introduction. Please clarify.

• Author's response: We thank the reviewer for highlighting this issue, which was also raised by the first reviewer. Accordingly the text of the manuscript was revised to clarify that in this study CAM referred to natural CAM products, including herbs, vitamins and minerals and probiotics. The following text was added: 'The United States (US) National Center for Complementary and Integrative Health (NCCIH) divides CAM into two main categories: (1) natural CAM products, such as herbs, vitamins and minerals and probiotics; and (2) mind and body therapies, most common of which are yoga, chiropractic and osteopathic manipulation, meditation, and massage therapy2. In this manuscript, CAM refers to natural CAM products.' (Page 4, lines 6-11)

2.5 I do ask authors to score the knowledge as a 10-item scale and then assess the association of knowledge score among the socio-demographic categories of participants.

• Author's response: As recommended by the reviewer, knowledge was scored as a 10-item scale and the associations of knowledge score with the socio-demographic characteristics of participants

were examined using simple and multiple linear regression analyses. The text of the various sections of the manuscript was revised to reflect the additional analyses.

2.6 Recruitment/response rates: it could be clearer as to how the pharmacists were invited/recruited to participate in the study, what you did to maximize the response rate, did the participant completed the questionnaire in the presence of researcher and how long would participant take to complete the questionnaire? The setting of the study was community pharmacies what about different pharmacy location as hospital pharmacists therefore the title of the manuscript should include community "… community pharmacists….."

• Author's response: As suggested, further details were included in the revised manuscript, as follows: 'Data collection took place in the selected pharmacies. Through face-to-face interviews with the pharmacists, a multi-component questionnaire was completed. Each interview lasted 10-15 minutes. The interviews were conducted by field workers who received extensive training on professional interviewing techniques and administration of the questionnaire prior to the start of the study. Interviewers were specifically trained to clearly explain the purpose of the study and the potential benefits of its results for the pharmacy profession and the health and wellbeing of the patients, hence increasing the interest of pharmacist in participation and improving response rate.'

In addition, and as recommended by the reviewer, the title of the manuscript was revised to indicate 'community pharmacists' instead of 'pharmacists'. (Page 6, lines 24-32)

2.7 Statistical analysis: Descriptive statistics is insufficient for this kind of studies you need to score the knowledge and or beliefs and to compare the median scores as appropriate

• Author's response: This comment was also raised by the two other reviewers of this manuscript, and was answered as follows: 'According to reviewers comment, additional data analyses were conducted to supplement the descriptive findings. More specifically, the knowledge questions were scored as 10-item scale and the associations of this knowledge score among the socio-demographic categories of participants were evaluated using simple and multiple linear regression. The text of the various sections of the manuscript was revised to reflect the additional analyses.

(3) Discussion

3.1 When comparing findings on knowledge, it is not clear how similar/different your knowledge measure was with other published findings. Please refer to literature and find similar studies conducted nearby in the region as Palestine, Jordan, Qatar and Iran also away in the US, Australia Singapore and then compare your findings with those relevant studies

• Author's response: As suggested by the reviewer, the findings related to knowledge were compared to other studies in countries of the region and elsewhere. Accordingly the text was modified as follows: 'The knowledge deficiencies found in this study were also reported by many other studies in the region such as Saudi Arabia,6,23Abu Dhabi,24 Jordan,19 Kuwait,20,21 Oman,22 Qatar,38 Palestine,41,42 and Iran43 as well as other countries such as Ethiopia,3 USA,18 Singapore,37 and in Trinidad and Tobago,44 and therefore appear to be a concern of global nature.'(Page 13, lines 18-24).

3.3 . Throughout the paper, you switch back and forth between CAM and herbals (one CAM modality). In addition, you only measured herbal knowledge and not CAM knowledge; therefore, some discussion points may be misleading/confusing. Much of your discussion focuses on herbal findings (including the knowledge measure) and should be situated in that context. Please be clear throughout

• Author's response: We thank the reviewer for the feedback. Accordingly the manuscript was revised to indicate that, in this paper, CAM refers to CAM products, which includes but is not limited to herbal

remedies. We have added a short definition of CAM at the beginning of the introduction section and have clarified it comprises natural CAM therapies including herbs, vitamins, minerals and probiotics. We also understand that the absence of the questionnaire utilized in this study could confuse the reader into thinking that we only included questions about herbal knowledge. We have now added the questionnaire which clearly reveals the incorporation of questions on vitamins (B&C), Omega 3, etc. Hope this clarifies the scope of this study.

Minor Typos:

Throughout the manuscript you should be consistent for example Health care or healthcare or health-care Table 1: Title pharmacists should be replaced by pharmacies

• Author's response: The text was modified as per the reviewer's recommendations.

Reviewer # 3. Professor Peter Bai James

(1) Introduction:

1.1 Paragraph 1 line 16: According to the World Health Organization (WHO), in developing countries, 65-80% of the population depends essentially on plants for primary health care.3, Please provide the scientific basis for this statement that is based on a recent original research or systematic review of the available literature or report. The current reference is not appropriate

• Author's response: Unfortunately there exists no updated reference for this statement. Therefore it was revised to reflect more recent data, as follows: 'Prevalence rate as high as 70% were reported for natural CAM products' use among the general population in various countries such as Canada and Kuwait.4,5 (Page 4, lines 13-15)

(2) Methods

2.1 With regards to the questionnaire, what informed its design in the first place and what also informed the inclusion of the question of how long the pharmacy opens?

• Author's response: These two comments were also raised by the first reviewer and were answered as follows :

o The design of the questionnaire used in the data collection for this study was informed by a thorough review of relevant past literature and by careful examination of the local context.16,23,24,34 (Page 7, lines 1-3).

o The question 'how long was the pharmacy open' was included because in the local context, the longer the duration the pharmacy has been opened for, the more likely its clientele would develop a more personalised relationship with the pharmacist allowing for a better communication of their health needs and concerns. (Page 7, lines 16-19).

2. 2 I have some issues with the inclusion of pilot data into the main study data based on the fact that no changes were made to survey tool. The essence of piloting a study is not just to see if the survey tool is adaptive to the local setting. Piloting a study assesses the 1.the process of conducting the study with regards recruitment, non-response. It looks at whether the inclusion criteria is sufficient or too restrictive 2. it also assesses the time and resource problems as well as(3) data management issues. All these issues in addition to others logistical issues can influence the nature of the pilot data collected and eventually the main study. Except the authors are stating categorically that no changes were made with regards every aspect of the pilot study including ones not normally reported in research papers, then their claim can stand. As researchers, we know that there are scientific and

logistical challenges that come to light when piloting a study which informs the way process in which the main study is done and as such informs the nature of the data collected. As such the way and manner in which the final study would have been conducted would be different compared the to the pilot study and that has the tendency to influence the data collected, results got after data analysis and conclusion made based on those findings. Another issue is that , the non-probability sample method was used to collect data from the 16 pharmacists for the pilot study whereas the in the main study probability sample method was used. It is difficult to understand how data collected from different sampling methods can be used together in the final analysis.

• Author's response: We thank the reviewer for his detailed comment and for raising important issues with regards to the inclusion of the pilot test data. Accordingly, data analyses for this study were re-conducted, removing the 16 questionnaires that were collected during the pilot test. The text of the Methods section was revised and the following sentence was added 'Data collected during the pilot testing of the questionnaire were not included in this study'. (Page 8, lines 5-6)

2.3 . Authors need to elaborate on how outcome variables were measured and what statistical tests were used to analyze the data Results 1.I see only descriptive statistics were done. It would have been good to see some inferential statistical analysis done. e.g one might want to know how CAM knowledge among pharmacist is influenced by their socio-demographic characteristics like age, qualification, level of experience, prior knowledge about CAM etc. As it stands now what is presented is good but not enough. some inferential statistics should be done.

• Author's response: This comment was also raised by the two other reviewers of this manuscript, and was answered as follows: 'According to reviewers comment, additional data analyses were conducted to supplement the descriptive findings. More specifically, the knowledge questions were scored as 10-item scale and the associations of this knowledge score among the socio-demographic categories of participants were evaluated using simple and multiple linear regression. The text of the various sections of the manuscript was revised to reflect the additional analyses.

(3) Discussion

The study reports that pharmacist in Lebanon often provides advice on the safe use of CAM products but their knowledge on the safety of CAM product is limited. It begs the question as to what type of advice is given and how that influenced patient health outcome. It will be good if the implications of the above anomaly are discussed.

• Author's response: We thank the reviewer for this interesting reflection. The question you raise is one of the main motivations for the authors to carry out this study. Despite the good intentions of community pharmacists to provide the best evidence based advice to their customers, the study unearthed some knowledge deficiencies that need to be addressed. With the absence of CAM professional development and training programs, the advice of pharmacists would be suboptimal and could, in some instances jeopardize the health and wellbeing of the patients. The study thus, raises the awareness of pharmacists, the Order of Pharmacists and the MoPH (among other stakeholders) on the importance of enhancing the education and knowledge of pharmacists as a means to improve public safety. Such enhancements should preferably be incorporated into the pharmacy educational programs particularly in light of the findings of this study that education is a significant predictor of CAM knowledge. The other challenge relates to patients' outcomes, as our study reveals, pharmacists rarely report toxic and undesirable side effects of CAM products to concerned parties. This is why the authors call for the creation of a responsive regulatory framework to ensure the safe integration and use of CAM products in Lebanon. The text of the manuscript was revised to further emphasize the aforementioned discussion.

Additional reviewers' comments from the pdf file of the manuscript

1- Page 4, lines 25-26: what do you mean? how does decision making process linked to use of CAM? Please re write this statement to make it more comprehensible

• Author's response: The sentence was written to clearly indicate the reasons for using CAM as follows: 'Such a widespread use of CAM could be attributed to dissatisfaction with conventional medicine, the increasing cost of conventional medical care, placebo effect, and the desire to be involved in the decision-making process related to one's health.7,8' (Page 5, line 19-20

2- Page 9, lines 15-16: Please revise this sentence. It does not read well.

• Author's response: The sentence was revised for clarity 'It is worth noting that 60.3% of pharmacists reported frequently checking for CAM product-drug interaction prior to selling the product. (Page 10, lines 14-16)

3- Page 11, lines 19-22: I do not see how these two sentences are linked. Please revised

• Author's response: The text of the Discussion was revised in line with the reviewer's comment. (Page 11,lines 19-2)

4- Page 11, lines 38-39: This does not read well

• Author's response: The sentence was revised to read as follows: 'Perhaps one of the most disconcerting findings of this study related to the deficiencies in the pharmacists' knowledge of CAM-drug interaction and to a lesser extent CAM products side effects.' (Page 13, lines 11-13)

5- Page 11, lines 45-52: I understood what the authors are trying to say but the sentence is long and does not read well

• Author's response: In response to the reviewer's comment, the sentence was revised to read as follows: 'One possible explanation for the observed knowledge deficiencies could be due to the biased information propagated by some CAM product companies. This information usually aims to maximize sales and neglect any factor that can affect the promotion of their products'. (Page 13, lines 21-24)

6- Page 12, line 53: This findings reported are only true for the Lebanon context. Please revise

• Author's response: The text was revised as per the reviewer's recommendation and the 'elsewhere' was deleted from this sentence and from the Conclusion section of the abstract.

VERSION 2 – REVIEW

REVIEWER	Carolina Oi Lam Ung State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao
REVIEW RETURNED	11-Oct-2018

GENERAL COMMENTS	Dear Authors, Please kindly see my additional comments: 1. CAM, by definition given by the authors in the first sentence of the Introduction, refers to the systems, practices and products.

	The same “CAM” is also used to refer to products in other parts of the manuscript. Please revise to avoid confusion. 2. Further confusion arises as the terms “CAM” and “CAM products” were used in different parts of the manuscript. For example in Abstract, the objective referred to CAM, section 2 of the questionnaire referred to CAM but section 3 and 4 of the questionnaire referred to CAM products. All the findings, however, related to CAM products. Another example would be the first paragraph of Introduction whereby the terms “CAM”, “CAM products” and “natural products” were used. Please clarify. 3. In Line 25, please justify the argument “One possible explanation for the observed knowledge deficiencies could be due to the biased information propagated by some CAM product companies.” 4. The findings in the statement “As for the pharmacists’ beliefs related to the CAM market in the country, a sizable proportion of survey participants (74.2%) were not sure about the quality of commercially marketed CAM products in Lebanon, whereby 41.9% were disagreeing or strongly disagreeing and 32.3% were neutral.” is different from those shown in Table 3. Please confirm all the findings presented in this manuscript. 5. In the questionnaire, some of the questions are double-barrelled (e.g. “Information resources on CAM products are available and easily accessible to the pharmacist “, “CAM products available in the Lebanese market are well standardized and of good quality “ and some not be specific enough (e.g. “The market for CAM products in Lebanon is well regulated“). The definition of CAM products was also not provided in the questionnaire. Please explain how the validity and the reliability of the survey were ensured in order to optimize the quality of the findings. 6. Please clarify “Pharmacists do not only believe in the utility of CAM products…” 7. Please clarify if “toxic” effects refer to adverse effects. 8. Line 16 on Page 10, please explain why pharmacists reported toxic effects to “pharmacists”. 9. Please do proper citation in the manuscript. 10. Please conduct proof reading by a native English speaker is recommended.

REVIEWER	Peter Bai James Australian Research Centre in Complementary and Integrative Medicine, Faculty of Health, University of Technology, Sydney
REVIEW RETURNED	08-Oct-2018

GENERAL COMMENTS	The authors have addressed most of my concerns. However, they failed to address some key issues which are:

	1. the authors failed to clearly describe how self knowledge of CAM was measured . what they presented is still scanty and incomplete. What was the score given to those that get the correct answer and those that got the wrong answer?. What score was given to those that answered "I don't know"? What was the minimum and maximum score and were the scores for each participant summated? If so, what was the cut-off summated score that was used to determine whether a participant was knowledgeable or not? 2. Can the authors explain why they failed to provide result of regression analysis that they supposedly said they did. I believe that result is important and must be presented Minor comment 3. Please reformat the in text citation of fourth paragraph of methodology(page 7 line 34.

VERSION 2 – AUTHOR RESPONSE

Reviewer 3 (Prof Peter Bai James)

1. Clearly describe how self knowledge of CAM was measured. What they presented is still scanty and incomplete. What was the score given to those that get the correct answer and those that got the wrong answer?. What score was given to those that answered "I don't know"? What was the minimum and maximum score and were the scores for each participant summated? If so, what was the cut-off summated score that was used to determine whether a participant was knowledgeable or not?

• Author's response: In line with the reviewer's recommendation, the following text was added to the Methods section 'Pharmacists were assigned a score value of '1' for any specific question which they have answered correctly and '0' if their answer was wrong. An 'I don't know' answer was also given a '0' because it reflected lack of knowledge. For each pharmacist, the assigned values for all questions were summed to obtain their respective knowledge score. Given that the questionnaire included 10 questions to evaluate self-knowledge the score could range between a minimum of 0 and a maximum of 10. The resulting score was considered as a continuous variable with higher values indicating better knowledge'. (Page 8, lines 9-16)

In addition, the minimum, maximum and mean ± SD values of the score in the study population were added to the results section, as follows 'Overall the score ranged between 1 and 9 in the study population, with a mean ± SD of 5.32 ±1.43'. (Page 11, lines 11-12).

2. Can the authors explain why they failed to provide result of regression analysis that they supposedly said they did. I believe that result is important and must be presented

• Author's response: As per the reviewer's request, table 6 was added to the manuscript to describe the results of the regression analysis.

3. Please reformat the in text citation of fourth paragraph of methodology (page 7 line 34).

• Author's response: The text was modified as per the reviewer's recommendation.

Reviewer: 1 (Reviewer Name: Carolina Oi Lam Ung)

1. CAM, by definition given by the authors in the first sentence of the Introduction, refers to the systems, practices and products. The same "CAM" is also used to refer to products in other parts of

the manuscript. Please revise to avoid confusion. Further confusion arises as the terms “CAM” and “CAM products” were used in different parts of the manuscript. For example in Abstract, the objective referred to CAM, section 2 of the questionnaire referred to CAM but section 3 and 4 of the questionnaire referred to CAM products. All the findings, however, related to CAM products. Another example would be the first paragraph of Introduction whereby the terms “CAM”, “CAM products” and “natural products” were used. Please clarify.

• Author’s response: We thank the reviewer for raising this issue to our attention. As recommended, the different sections of the manuscript were revised to indicate ‘CAM products’ rather than ‘CAM’. ‘CAM’ was only used when reference was made to the all types of CAM.

3. In Line 25, please justify the argument “One possible explanation for the observed knowledge deficiencies could be due to the biased information propagated by some CAM product companies.”

• Author’s response: As recommended by the reviewer, the following justification was added for this argument, as follows: ‘A few studies showed that personal sale visits of certain products’ companies to pharmacists (called “detailing”) could drive prescriptions in favor of the product being promoted. This is true even though pharmacists’ may be aware of the potential conflict of interest these visits precipitate (Kamal et al., 2015; Hajjar et al., 2017; Manchanda et al., 2005)’. (Page 13, lines 1-5).

4. The findings in the statement “As for the pharmacists’ beliefs related to the CAM market in the country, a sizable proportion of survey participants (74.2%) were not sure about the quality of commercially marketed CAM products in Lebanon, whereby 41.9% were disagreeing or strongly disagreeing and 32.3% were neutral.” is different from those shown in Table 3. Please confirm all the findings presented in this manuscript.

• Author’s response: As recommended by the reviewer, the text was revised for clarity and consistency. (Page 10, lines 1-3).

5. In the questionnaire, some of the questions are double- barreled (e.g. “Information resources on CAM products are available and easily accessible to the pharmacist “, “CAM products available in the Lebanese market are well standardized and of good quality “ and some not be specific enough (e.g. “The market for CAM products in Lebanon is well regulated“). The definition of CAM products was also not provided in the questionnaire. Please explain how the validity and the reliability of the survey were ensured in order to optimize the quality of the findings.

• Author’s response: Thank you for pointing out this issue. We concur with the reviewer that the two double barreled questions could have been preferably broken into two questions each. The authors did not do so in this study to keep the number of questions low with the assumption that an answer of yes to each of the two questions meant yes to the full statement, e.g. “available and easily accessible” and an answer of no is meant to be no for the full statement. Regretfully, this was not picked up during the pilot testing phase and thus was not corrected for prior to data collection. We have added the following statement to the shortcoming section “A couple of questions in the questionnaire were double barreled and could have been better broken into two questions each to ensure clarity and accuracy of answer”. (Page14, lines 32-33).

The question on the regulation of CAM products was well understood by pharmacists during both the pilot testing and data collection phases since this relates to an ongoing national discussion on the role of Ministry of Health and Population in regulating CAM products to protect public safety.

The questionnaire used in this study was developed by a multi-disciplinary expert panel including a pharmacist/academician, a nutrition expert, a health management and policy expert and a statistician. The group met several time and deliberated the questionnaire until consensus on the final version was reached. The final version was pilot tested on 16 pharmacists and necessary corrections were introduced to the questionnaire to enhance clarity and accuracy.

6. Please clarify “Pharmacists do not only believe in the utility of CAM products…”

• Author’s response: The text was classified as follows: The results of this study showed that pharmacists believed in the utility of CAM products and were willing to assume a leading role by asking for exclusive rights to sell CAM products in pharmacies and under the advice of community pharmacists. (Page12, lines 4-6).

7. Please clarify if “toxic” effects refer to adverse effects.

• Author’s response: Yes, in this paper toxic effects and adverse effects were used interchangeably. To avoid confusion, the manuscript was revised and only the term ‘adverse effects’ was used.

8. Line 16 on Page 10, please explain why pharmacists reported toxic effects to “pharmacists”.

• Author’s response: In this study, 234 out of 310 surveyed pharmacies had more than one pharmacist working in them. A couple of pharmacists reported the toxic effects to other pharmacists working with them in the same pharmacy. The text of the results was revised to explain this finding. (Page 10, lines 23-24).

9. Please do proper citation in the manuscript.

• Author’s response: The text was modified as per the reviewer’s recommendation.

10. Please conduct proof reading by a native English speaker is recommended

• Author’s response: The manuscript was read and edited by a native English speaker.

VERSION 3 – REVIEW

REVIEWER	Carolina Oi Lam Ung Lecturer (Macau Fellow), State Key Laboratory of Quality Research in Chinese Medicine, Institute of Chinese Medical Sciences, University of Macau, Macao
REVIEW RETURNED	26-Dec-2018

GENERAL COMMENTS	Thank you very much for the revision. The manuscript in the current form is much clearer and present some important findings from Lebanon. There are a few typos which you need to attend to: 1. Line 8, Page 10 – “availabilibarrety” 2. Line 16, Page 12 – “on the front” => “On the front” 3. Line 5, Pate 14 – “another” => “Another” Again, it was a pleasure to review your work.

REVIEWER	Peter Bai James University of Technology, Sydney Australia
REVIEW RETURNED	23-Dec-2018

GENERAL COMMENTS	The authors have addressed my concerns Just a minor comment

	1. Please indicate the cut-off summated score that was used to determine whether a participant was knowledgeable or not Please provide an interpretation of the beta coefficient 0.68(0.29,1.07) in the result section

VERSION 2 – AUTHOR RESPONSE

Reviewer 3 (Prof Pete Bai James)

1. Please indicate the cut-off summated score that was used to determine whether a participant was knowledgeable or not

• Author's response: In response to the reviewer's comment. We have indicated in the revised manuscript that the knowledge score was used as a continuous variable with no specific cutoff, whereby higher scores reflected better knowledge. (Page 8, lines 15-16).

2. Please provide an interpretation of the beta coefficient 0.68(0.29,1.07) in the result section

• Author's response: As per the reviewer's recommendation, the text was revised to provide an interpretation of the association as follows 'After adjustment for covariates, receiving education/training on CAM products during university was also positively correlated with higher knowledge score (ß=0.68, 95%CI: 0.29-1.07); that is, receiving any education/training on CAM-products increases the mean knowledge score by 0.68 while adjusting for socio-demographic characteristics." (Page 11, lines 15-19).

Reviewer: 1 (Reviewer Name: Carolina Oi Lam Ung)

1. Minor comments: 1)Line 8, Page 10 – "availabilibarrety"; 2) Line 16, Page 12 – "on the front" => "On the front;3) Line 5, Pate 14 – "another" => "Another"

• Author's response: The text of the revised manuscript was edited as per the reviewer's comments.