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Research / Araştırma Makalesi

Evidence-Based Bibliometric and Scientometric Analysis of Research on Casein Phosphopeptide Amorphous Calcium Phosphate

Kazein Fosfopeptit Amorf Kalsiyum Fosfat Araştırmasının Kanıta Dayalı Bibliyometrik ve Scientometrik Analizi

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ABSTRACT

Backgrounds: To review the research model on the use of CPP-ACP in preventive dentistry with the bibliometric analysis method.

Methods: A comprehensive search of the Web of Science database for literature on CPP-ACP was conducted between 1999 and 2020.Information such as citations, bibliographic data, and keywords was extracted using different keyword combinations (“casein phosphopeptide-amorphous calcium phosphate ” OR ‘’ calcium phosphopeptide-amorphous calcium phosphate’’ OR “CPP-ACP”).The analysis and visualization of the selected documents and related data were carried out using MS Excel and VOSviewer software. VOSviewer was used to create graphical representations of the data and network graphs were created to assess the various associations between research themes, countries, organizations, authors, journals, and citations.

Result: The search yielded 556 documents of which 356 were chosen for analysis. The results showed that the first most cited publication was published in 2003 and received 292 citations. Also,12 publications published in 2011 received the most citations among all publications. Among 30 countries, Australia contributed the most with 29 articles. The top 100 most cited articles in CPP-ACP were published in a total of 32 journals.

Conclusion: CPP-ACP is a popular topic and publications have continued to increase from past to present. The bibliometric analysis provides information on the top 100 most cited CPP-ACP papers and their citation details, as well as contributing authors, countries and organisations.

Keywords: Bibliometric analysis, Casein phosphopeptide-amorphous calcium phosphate, CPP-ACP, Dental caries, Fluoride

ÖZ

Amaç: Kazein fosfopeptit amorf kalsiyum fosfat (CPP-ACP)'ın diş dokularındaki remineralizasyon özelliği sayesinde koruyucu diş hekimliğinde kullanımı hızla artmıştır. Dolayısıyla bu konudaki çalışmalar da ivme kazanmıştır. Bu çalışmanın amacı CPP-ACP ile ilgili makaleleri niceliksel ve niteliksel değerlendirip, bibliyometrik bir yaklaşım kullanarak analiz etmeyi amaçlamıştır.

Gereç ve Yöntemler: CPP-ACP ile ilgili literatür için Web of Science veri tabanında 1999-2020 yılları arasında kapsamlı bir arama yapılmıştır. Farklı anahtar kelime kombinasyonları ("kazein fosfopeptid-amorf kalsiyum fosfat" VEYA ‘’kalsiyum fosfopeptid amorfoz kalsiyum fosfat’’ VEYA "CPP-ACP") kullanılarak atıflar, niteliksel-niceliksel veriler ve anahtar kelimeler gibi bibliyografik bilgiler dışa aktarıldı. Kriterleri karşılayan verileri analiz etmek için MS Excel yazılımı ve görselleştirme için VOSviewer yazılımı kullanılmıştır. Bibliyometrik veriler arasındaki ilişkileri değerlendirmek için VOSviewer yazılımı ile ağ grafikleri oluşturulmuştur.

Bulgular: Literatür aramasında 556 doküman elde edilmiş ve kriterleri sağlayan 356'sı analiz edilmiştir. En çok atıf alan ilk yayının 2003 yılında yayınlandığı ve 292 atıf aldığı görülmüştür. Tüm yayınlar arasında en çok atıf alan yayınlar 2011 yılında yayınlanan 12 yayın olmuştur. Toplamda 30 ülke arasında Avustralya 29 makale ile en çok katkıda bulunan ülke olmuştur. CPP-ACP'de en çok atıf alan ilk 100 makale toplam 32 dergide yayınlanmıştır.

Sonuç: CPP-ACP popüler bir konudur ve geçmişten günümüze yayınlar artarak devam etmiştir. Bibliyometrik analiz çalışması, en çok atıf alan ilk 100 CPP-ACP makalesi ve bunların atıf detaylarının yanı sıra katkıda bulunan yazarlar, ülkeler ve kuruluşlar hakkında bilgi sunmaktadır.

Anahtar Kelimeler: Bibliyometrik analiz, CPP-ACP, Diş çürükleri, Florid, Kazein fosfopeptit-amorf kalsiyum fosfat

Introduction

Dental caries is caused by the demineralization of tooth hard tissue by organic acids formed as a result of the fermentation of carbohydrates by cariogenic bacteria.[1,2] In which direction the dynamic balance between demineralization and remineralization events is disturbed, that process becomes active. Loss of calcium and phosphate from the subsurface enamel leads to the onset of demineralization and subsurface lesion formation.[3] In the early stage, caries lesions are reversible as a result of the diffusion of calcium and phosphate ions to the subsurface lesions and remineralization, and the lost mineral content is regained.[4] In light of this information, new or alternative approaches were needed to control the remineralization process and cariostatic activity, especially in pediatric patients.[1,5]

Epidemiological studies have shown that milk consumption is lower in children with a high incidence of dental caries than in those with a low incidence of dental caries.[6,7] Milk is a protein-rich food and contains factors with anti-cariogenic properties such as calcium, phosphate, casein, and lipids.[6,7] Casein is the predominant phosphoprotein, accounting for 80% of the proteins in bovine milk, found in microcellular complexes. Casein phosphopeptides (CPP) stabilize calcium and phosphate ions in a soluble form called amorphous calcium phosphate (ACP).[4]

Laboratory studies in animals and humans have shown that CPP-ACP nano complexes have anti-cariogenic potential.[8-10] CPP promotes the remineralization process by binding to pellicles and plaque and stabilizing high concentrations of calcium and phosphate ions together with fluoride ions on the enamel surface into CPP-ACP complexes.[10] Thanks to this property, it has found many uses in dental practice. It can also be used to reduce dental erosion caused by gastritis, reflux, or other diseases, to minimize decalcification after orthodontic treatments, to repair enamel in white spots, in fluorosis, and sensitive teeth (e.g., to reduce hypersensitivity caused by a whitening procedure or sensitivity on an exposed root surface after professional teeth cleaning) or the prevention of caries in high-risk patients.[7]

All of its advantages have led researchers to investigate the use of CPP-ACP in dentistry, and there has been exponential growth in research on this topic. A comprehensive systemic analysis would be appropriate to evaluate and analyze current research both quantitatively and qualitatively. The bibliometric analysis provides a quantitative and reliable review of the literature in any field of research, identifying

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countries, organizations, and authors associated with the topic based on the citation frequency of the research conducted.[11,12] Bibliometric indicators help researchers and organizations assess and compare the impact of articles by observing research outputs and citation data from other scientific works.[13,14] This method has been applied to several areas of pediatric dentistry, but bibliometric analysis of articles focusing on CPP-ACP complexes and their effects has not been published. Therefore, this study aimed to analyze CPP-ACP-related articles in dentistry using a bibliometric approach.

Material and Methods

Research Type

Analytical research from quantitative studies

Research Time and Place

To identify relevant research in the field, a comprehensive systematic literature review was conducted on 25.06.2023 through Web of Science, an online database using the Clarivate search engine. Bibliographic information related to citations, authors, keywords, countries, and other relevant information was extracted. The search strategy was as follows in all fields, including the database: Search terms were combined by "OR": "casein phosphopeptide-amorphous calcium phosphate'' OR ''calcium phosphopeptide-amorphous calcium phosphate" OR ''CPP-ACP''.

Population and Sample of the Study

Ethical standards were adhered to in this study. Ethical approval was not required because the study used bibliometric data from the Web of Science (WoS) database. The search for the same criteria was repeated 3 times at different times to avoid bias. A total of 556 documents were retrieved in the search. Some inclusion and exclusion criteria were applied to obtain the most comprehensive and relevant data. For this purpose, all articles were manually screened for inclusion. No geographical region, language, or time (date) filters were applied. However, proceeding papers, editorial material or letters, notes, and early access articles were excluded. The Dentistry Oral Surgery Medicine category was selected from the Web of Science research areas categories. Finally, 356 records were selected for bibliometric analysis.

Data Collection

These were sorted from most cited to least cited. The first 100 of the 356 most cited documents were exported via Excel. The articles listed as a result of the search criteria were published between 1999 and 2020. Information about these articles such as title, first author, number of authors, institute/country, journal name, year, citation, keywords, and abstract were recorded. The articles were ranked from the most cited to the least cited. When there were several articles with the same number of citations, the most recently published article was ranked higher. For articles published in the same year with the same number of citations, the one with fewer authors was ranked higher.

VOSviewer version 1.6.10 software (Centre for Science and Technology Studies, the Netherlands) with an automatic term identification algorithm was used to map the bibliometric network of the exported data (downloadable at www.vosviewer.com). Bibliometric indicators related to documents, citations, references, keywords, authors, organizations, and countries were examined. Bibliometric indicators related to documents, citations, references, keywords, authors, organizations, and countries were examined and co-occurrence networks and bibliographic couplings were visualized.

Results

Table 1 shows the top 10 most cited articles on CPP-ACP in descending order of the number of citations. **Figure 1** shows the top 100 most cited studies on CPP-ACP and the distribution of citations by year. The first most cited publication was published in 2003 and received 292 citations. Activity in CPP-ACP studies started in 2007 and onwards. Of the top 100 most cited articles, the highest number of publications (N = 13) occurred in 2009. Also, 12 publications published in 2011 received the most citations among all publications (673 citations).

Table 1. Top 10 of the 100 most cited articles in CPP-ACP based on the citation count

Rank	Authors	Research Article	Journal	Instutition (Corresponding author)	Times Cited, WoS Core	Times Cited All Databases	Year
1	Reynolds, EC; Cai, F; Shen, P; Walker, GD	Retention in plaque and remineralization of enamel lesions by various forms of calcium in a mouthrinse or sugar-free chewing gum	Journal of Dental Research	University of Melbourne	292	312	2003
2	Reynolds, EC; Cai, F; Cochrane, NJ; Shen, P; Walker, GD; Morgan, MV; Reynolds, C	Fluoride and casein phosphopeptide-amorphous calcium phosphate	Journal of Dental Research	University of Melbourne	233	253	2008
3	Shen, P; Cai, F; Nowicki, A; Vincent, J; Reynolds, EC	Remineralization of enamel subsurface lesions by sugar-free chewing gum containing casein phosphopepticle-amorphous calcium phosphate	Journal of Dental Research	University of Melbourne; Pfizer	197	217	2001
4	Cochrane, NJ; Saranathan, S; Cai, F; Cross, KJ; Reynolds, EC	Enamel subsurface lesion remineralisation with casein phosphopeptide stabilised solutions of calcium, phosphate and fluoride	Caries Research	University of Melbourne	176	180	2008
5	Iijima, Y; Cai, F; Shen, P; Walker, G; Reynolds, C; Reynolds, EC	Acid resistance of enamel subsurface lesions remineralized by a sugar-free chewing gum containing casein phosphopeptide-amorphous calcium phosphate	Caries Research	University of Melbourne; Nagasaki University	153	166	2004
6	Bailey, DL; Adams, GG; Tsao, CE; Hyslop, A; Escobar, K; Manton, DJ; Reynolds, EC; Morgan, MV	Regression of Post-orthodontic Lesions by a Remineralizing Cream The effect of casein phosphopeptide-	Journal of Dental Research	University of Melbourne	130	141	2009
7	Kumar, VLN; Itthagarun, A; King, NM	The effect of casein phosphopeptide-amorphous calcium phosphate on remineralization of artificial caries-like lesions: an in vitro study	Australian Dental Journal	Griffith University; University of Hong Kong	121	137	2008
8	Rajendran, R; Kunjusankaran, RN; Sandhya, R; Anilkumar, A; Santhosh, R; Patil, SR	Comparative Evaluation of Remineralizing Potential of a Paste Containing Bioactive Glass and a Topical Cream Containing Casein Phosphopeptide-Amorphous Calcium Phosphate: An in Vitro Study	Pesquisa Brasiliera Em Odontopediatria E Clinica Integrada	Saveetha Institute of Medical & Technical Science; Saveetha Dental College & Hospital;	114	114	2019
9	Morgan, MV; Adams, GG; Bailey, DL; Tsao, CE; Fischman, SL; Reynolds, EC	The anticariogenic effect of sugar-free gum containing CPP-ACP nanocomplexes on approximal caries determined using digital bitewing radiography	Caries Research	University of Melbourne; State University of New York (SUNY) System	109	121	2008
10	Rahiotis, C; Vougiouklakis, G	Effect of a CPP-ACP agent on the demineralization and remineralization of dentine in vitro	Journal of Dentistry	National & Kapodistrian University of Athens	109	124	2007

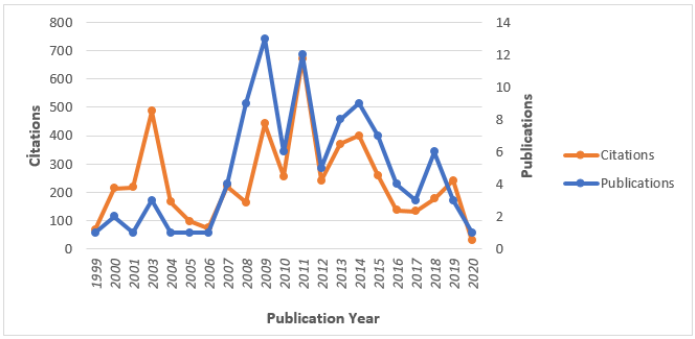

Figure 1. Publications and citation trends in CPP-ACP over a period of 1999-2020

The country analysis using VOSviewer showed that 30 countries have contributed to research and publications in this field, with/without collaborations. **Figure 2** presents country contributions and bibliographic coupling. Australia was the highest contributing country with 29 articles. The top 100 most cited articles in CPP-ACP were published in a total of 32 journals. The 1st journal with the highest number of article contributions was the Journal of Dentistry (28%), the 2nd journal was Caries Research (13%), and the 3rd one was the Australian Dental Journal (10%) (**Figure 3.**).

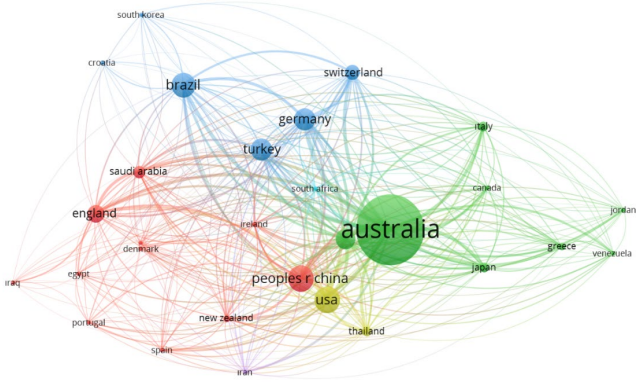

Figure 2. Contribution to the literature based on countries and bibliographic coupling

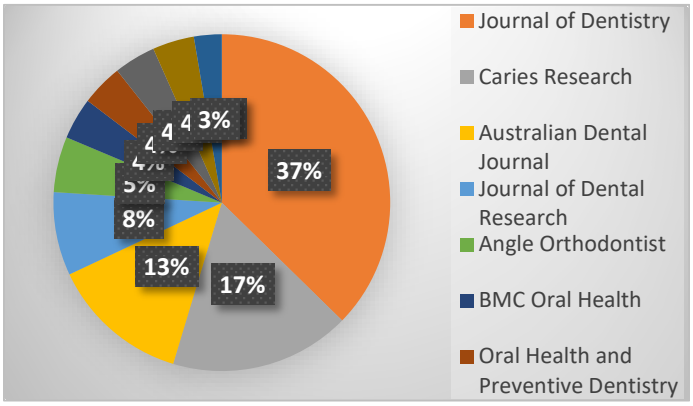

Figure 3. The journals in which the 100 most-cited articles were published

Different 83 researchers provided first-author contributions to the 100 most cited articles. The first author with the most-cited articles was Reynold EC. with a total of 583 citations in 3 articles followed by Shen Peiyan with a total of 335 citations in 4 articles in the field of the subject (**Figure 4.**). After analyzing these most cited authors in more detail, it was found that Reynolds EC, Shen Peiyan, and Reynolds E contributed to other research articles as co-authors 20, 11, and 9 times, respectively. **Figure 5** presents the cocitation network of authors in CPP-ACP research between 1999 and 2020. The 18 authors with the most cocitations are shown. In the figure, the node size represents the number of articles published by each author, and the joining lines represent the strength of collaborations among authors.

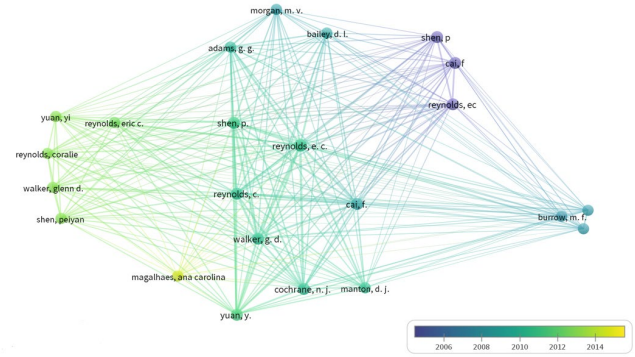

Figure 4. Author and co-author contribution with their network in the top-cited articles

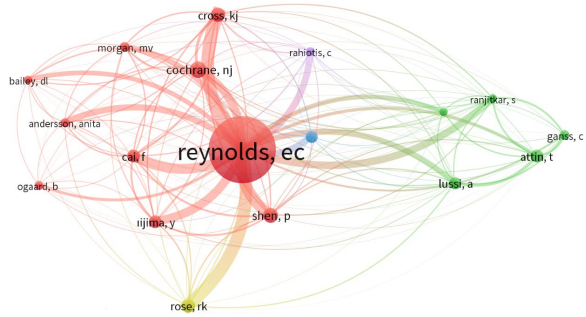

Figure 5. Cocitation network of authors 18 met the threshold

A total of 166 different keywords were identified in the top 100 most cited studies. The top 10 most frequently used keywords and the number of times these words were in the included articles are given in **Table 2.** The first 3 most frequently used keywords were CPP, fluoride, and remineralization, respectively. In addition, the visualization of the keyword co-occurrence density of the 100 most cited articles is presented in **Figure 6.**

Table 2. The most frequent used keywords in top-cited articles

Serial No	Keywords	Frequency
1	CPP-ACP	35
2	Fluoride	27
3	Remineralization	19
4	Enamel / Tooth enamel	18
5	Casein Phosphopeptide-Amorphous Calcium Phosphate	17
6	Enamel demineralization/ demineralization	17
7	Caries / Dental caries	15
8	Erosion/Enamel erosion/tooth erosion	15

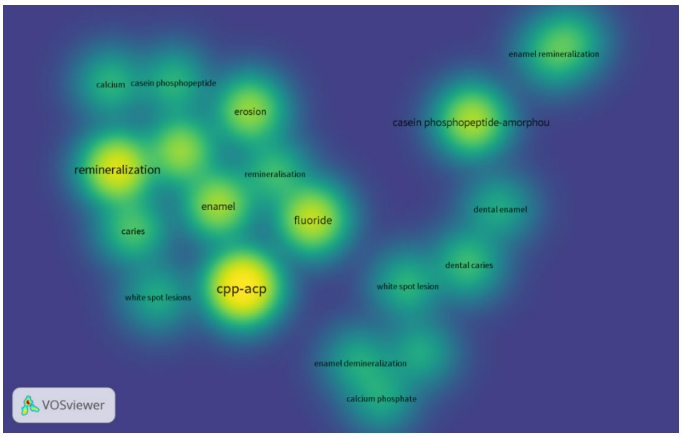

Figure 6. Keyword co-occurrence density visualization of the 100 top-cited articles

Discussion

This bibliometric study is the first to analyze the 100 most cited papers in the CPP-ACP field and their main characteristics. It has been considered that a highly cited article can have an important place in the field of health and can influence clinical research and practice.[15] Therefore, this bibliometric study not only presents a historical development of scientific progress in preventive dentistry but also shows trends and gaps in research developments.

While evaluating the performance of a scientific work based on citation counts, some characteristics should be taken into consideration. These variables include the field of specialization, the prestige of the journal, open access, number of co-authors, type of document, and social network of authors.[16,17] Thomson Reuters Web of Science (WoS) is a comprehensive publication database containing publications from 1945 to the present and providing citation metrics,[18] but there are other platforms used for academic search.

To avoid this, the present study, similar to Erdinç's study, used WoS to analyze articles and Google Scholar to verify the number of CPP-ACP related citations.

As Google Scholar includes citations from theses, conference reports, preprints and books; this results in higher citation counts.[19] To avoid this, the present study, similar to Erdinç's study[20], used WoS to analyse articles and Google Scholar to verify the number of CPP-ACP related citations.

A pilot study was made to reveal the time when research published in the scientific literature in the field of CPP-ACP began to appear. A safe approach has been maintained to avoid inadvertent omission of relevant publications. Although the first publication mentioning CPP-ACP was published in 1999,[21] no more than two articles per year were published until 2007. When the top 100 most cited articles were ranked, a list was formed from 1999 until the time the data was compiled and this article was written (i.e. June 2023). This article does not discuss the most cited articles' research contents and results. However, the top 100 articles were evaluated but to present to the readers, only the research contents and results of the 10 most cited articles described.

A potential limitation of the bibliometric analysis is that older papers have more time to receive citations. In this study, although the first article on the subject was published in 1999, the most cited (292 citations) article in the CPP-ACP fields was published by Reynolds EC. in 2003.[22] Therefore, it would be wrong to conclude that the oldest article received more citations. The objectivity, scope, and effectiveness of the article are more important factors. According to the results of the analysis, the top four most productive countries are Australia, China, the United States of America (USA), and Brazil. Australia ranked first in both the number of citations and number of publications. This could be attributed to the importance given to oral hygiene and preventive dentistry in Australia. Turkey was among the top 10 most productive countries and contributed to the scientific literature in this field.[23,24] As for the most productive organizations, the University of Melbourne led the way followed by the Universidade de Sao Paulo, Brazil, and the University of Hong Kong, China. In addition, it can be interpreted that the University of Melbourne, Australia is the most productive country and institution thanks to the presence of different researchers with common interests and fields of study. Consequently, 6 of the top 10 highly cited authors, namely, Reynolds EC. et al.,[22] Shen et al.,[8] Reynolds E.,[10] and Cochrane et al.[4] were affiliated with The University of Melbourne. Furthermore, through co-citations network analysis of authors, these authors have been identified as major contributors to research collaborations. In a bibliographic analysis, co-author network analysis helps to analyze the main areas of expertise in a field in terms of groups of authors co-cited in the relevant literature. This working group seems to have done the most work on our research topic. It is possible to see more collaborative projects from this working group in different fields.

In the years when the most cited papers were published, the number of co-authors in the published literature increased over time and the majority of papers had more than 3 authors. Some researchers contributed to the literature both as the first name and co-author in the list of the top 100 most cited articles. As the first author, 83 researchers contributed to the most cited articles. The first author with the most-cited articles was Reynold EC. followed by Shen Peiyan in the field of the subject (**Figure 5**.). After analyzing these most cited authors in more detail, it was found that Reynolds EC, Shen Peiyan, and Reynolds E contributed to multiple articles. The number of co-authors increased over time in the years when the most cited papers were published. This may be due to the widespread use of CPP-ACP in dentistry, and the interest of different researchers in institutes, countries and different researchers.

Journal of Dentistry (impact factor: 4.379) was the journal with the highest number of relevant articles (%28). The fact that the journal is a general dentistry journal, publishes articles on various topics, and is indexed in Science Citation Index may be attractive factors for researchers. The Caries Research Journal (impact factor:4.053), one of the journals with the most important articles on caries and caries prevention and indexed in SCI, was the second journal that published the most articles on CPP-ACP (13%). The use of CPP-ACP as an anti-caries agent by affecting the remineralization process may explain the 2nd most preferred choice of this journal. The 3rd journal with the highest number of relevant articles (10%) was The Australian Dental Journal (impact factor:2.291). The number of related publications decreased in journals ranked 4th and following in the ranking of journals in which the top 100 most cited articles were published (Figure 3). This situation can be associated with the use of CPP-ACP in different fields and the increase in the number and diversity of journals.

The most frequently used keywords in the included articles were also analyzed. The identified keywords will help them easily and quickly access CPP-ACP-related articles for future research. No keyword was found in 11 of the top 100 most cited articles.[21,25-33] The most frequent keyword was “CPP-ACP” followed by “fluoride” and then “remineralization”. Some of the top 10 most frequently used keywords are terms that appear to be generic keywords such as “enamel, caries, or casein phosphopeptide” (Table 2). Therefore, it seems that it may be useful to use general keywords related to remineralization and demineralization when searching for publications on CPP-ACP. Therefore, when searching for publications on CPP-ACP, it may be useful to use general keywords related to remineralization and demineralization rather than the specific use of the keywords casein or calcium phosphopeptide-amorphous calcium phosphate.

This study has some limitations. Firstly, a single database was used to collect bibliographic data. In future studies, more databases such as Scopus and Google Scholar can be included to search for articles. Secondly, one of the limitations of our study is that only the top 10 most cited articles were examined in detail and the findings and results of all included articles were not analyzed. Furthermore, in bibliometric analyses, research articles published in recent years are disadvantaged in terms of citation due to limited time, although they are more up-to-date.

Regardless of its limitations, this study on CPP-ACP will help future researchers to identify the most influential countries, universities, authors, journals, and keywords to identify possible avenues when

researching the topic and seeking collaborations.

Conclusion

This analysis showed that the number of publications was the highest between 2009 and 2014. This analysis also showed that Australia was the country with the highest number of participants in research on CPP-ACP, and the Journal of Dentistry was the journal with the highest number of publications.

Değerlendirme / Peer-Review

İki Dış Hakem / Çift Taraflı Körleme

Etik Beyan / Ethical statement

Bu çalışmanın hazırlanma sürecinde bilimsel ve etik ilkelere uyulduğu ve yararlanılan tüm çalışmaların kaynakçada belirtildiği beyan olunur.

It is declared that during the preparation process of this study, scientific and ethical principles were followed and all the studies benefited are stated in the bibliography.

Benzerlik Taraması / Similarity scan

Yapıldı – ithenticate

Etik Bildirim / Ethical statement

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Finansman / Grant Support

Yazar bu çalışma için finansal destek almadığını beyan etmiştir. | The author declared that this study has received no financial support.

Çıkar Çatışması / Conflict of Interest

Yazar çıkar çatışması bildirmemiştir. | The author have no conflict of interest to declare.

Yazar Katkıları / Author Contributions

Çalışmanın Tasarlanması | Design of Study: TTK (%100)
Veri Toplanması | Data Acquisition: TTK (%100)
Veri Analizi | Data Analysis: TTK (%100)
Makalenin Yazımı | Writing up: TTK (%100)
Makale Gönderimi ve Revizyonu | Submission and Revision: TTK (%100)

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