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## A Bibliometric Analysis of Quassinoids Research – A Class of Bioactive Compounds

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Quassinoids are a class of bioactive compounds that are obtained from the Simaroubaceae family. This family consists of more than 170 species of trees and bushes of pantropical distribution. Due to their potent bioactivity against chronic illness, the quassinoids are regularly explored for their biological activities. This has resulted in the buildup of scientific literature. Therefore, here we analyzed the global literature, indexed in SCI-E journals up to 2018 on quassinoids which is a triterpenoid natural group of compounds. There were a total of 793 publications with 16283 citations and 10724 citations without self-citation having an h-index of 56 and average citation per item of 20.53. We have also analyzed the year wise publication growth, most prolific authors, organizations and countries, most prolific journals, frequencies of keywords, and relevant terms of title and abstract. The authorship pattern and collaboration network between countries, authors, and languages of publication have also been analyzed. Overall, this compilation will help as an essential resource to refer to the detailed evidence regarding the quassinoids research.

**Keywords:** Citation, Mapping, Natural compound, Scientometric, Triterpenoid

### Introduction

Quassinoids are a group of natural compounds that are extracted from Simaroubaceae family of the plant kingdom. The Simaroubaceae family is comprised of 32 genera and over 170 species of bushes and trees of pantropical distribution. As a result of the biochemical variety determined and discussed for the member species of Simaroubaceae family, it's worth noting that this family can certainly be recognized as promising for the research on the bioactive molecules with amazing investigation potential. Nevertheless, a lot of its species haven't been studied or even remain unexplored. In this direction, the researchers are continuously searching the members of Simaroubaceae family for the potential of bioactive compounds like quassinoids. Structurally, quassinoids based on their structure skeleton have been grouped into five subtypes viz. C-18, C-19, C-20, C-22 and C-25. More than 150 quassinoids derivatives have been isolated to date.

Quassinoids are being used in traditional medicine for a long time.<sup>1</sup> Furthermore, it has also been claimed that a person named quasii cured fever from bark extract of a

tree which was later named after him as quassia. Due to their high biological activities and medicinal values, quassinoids have drawn the attention of researchers from the 20<sup>th</sup> century onwards and have been studied for many biological properties.<sup>2</sup> Quassinoids are reported as antimalarial, antifeedant, antileukemia, antiplasmodial, insecticidal, anti-inflammatory, anti-cancer, antiulcer, antipyretic, antifertility, anti-HIV, cytotoxic activities, and induction of murine stem cell differentiation. Moreover, quassinoids are reported to controls leishmanial parasites within the host macrophages.<sup>3-9</sup> For the benefit of clinical therapies of diseases mentioned above, pharmacological properties and mechanism of action of quassinoids are extremely important.

In recent years several publications on quassinoids have been published in which significant findings were reported. In this paper, the bibliometric method has been applied to investigate the published literature on quassinoids. Bibliometric or scientometric techniques are widely used to evaluate the scientific output of an individual researcher, research journals and periodicals, organizations and countries to evaluate quantitatively. Previously bibliometric analysis of some natural compounds, journals, institutions, and countries<sup>10-12</sup> has been investigated by a number of authors.

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Zhang *et al.* (2009)<sup>(13)</sup> evaluated research trends in volatile organic compounds using conventional bibliometric techniques. Whereas, Du and Tang (2014)<sup>(14)</sup> analyzed anti-cancer natural products using PubMed data. Recently, Yeung and El-Demerdash (2018)<sup>(15)</sup> analyzed the molecular responses of cancers by natural products by quassinoids by using a web of science (WOS) data. Yao *et al.* (2012)<sup>(16)</sup> mapped the literature on artemisinin using Medline and WOS data to reveal the global scientific production and trends of developing research trends on artemisinin research. The main objective of this study is to find out the trends in quassinoids research using scientometric techniques and to determine the yearly growth of literature, leading authors, journals, organizations, highly cited publications, authorship patterns, and collaboration dynamics.

## Materials and Methods

Data for this study was collected upto the year 2018 from Science citation index expanded (SCI-E) database of WOS core collection from Clarivate analytics, using the primary search feature on 20 August 2019. The keyword used is “Quassinoid” or “Ouassin” or “Quassinoids”. The document under the category of correction, reprint, and retracted publication were excluded from the study. There were a total of 798 publications in quassinoids indexed in SCI Journals and after removing retracted and correction 793 publications were chosen for this study. All the results were downloaded in MS-excel for analysis. For data visualization software VOSviewer version 1.6.15 was used.

## Results and Discussion

### Year Wise Publication

Year wise publications on quassinoids indexed in SCI journals reveal that there was only 1 publication in 1945 and for the next four years there was no literature published, and in the year 1950 there were two publications. For the following publication, there was a time lag of 4 years and up to 1972, there were 18 publications indexed in Web of science. From 1975 onwards there was continuous growth in publication on quassinoids and growth of literature was exponential. From 1975 to 1999, there were 372 publications, and from 2000 to 2018, there were 407 publications indexed in SCI journals (Fig. 1A).

### Authorship Pattern

Analysis of authorship patterns of quassinoids publications implicates that 97% of the 793

publications are written in co-authorship. Only 24 publications are written by individual authors. The most prevalent authorship pattern is four authors with 144 publications (18.15%) followed by two authors (135, 17.02%), five authors (122, 15.38%), three authors (108, 13.61%). There are sixteen publications written by 10 or more authors as given in Table 1 that depict hyper authorship in quassinoids research publications.

### Document Types

Data retrieved on quassinoids were categorized in 9 document types categories, *i.e.* article, note, review, meeting abstract, proceedings paper, letter, editorial material, correction, and also retraction. Document types correction (3 publications) and retractions (2 publications) were excluded from the study. The highest number of documents were articles (651, 82.09%) followed by note (48, 6.05%), review (45, 5.67%), meeting abstract (21, 2.64%), proceedings paper (17, 2.14%), letter (15, 1.89%) and editorial material (2, 0.25%).

### Languages of Publication

The 793 publications on quassinoids were published in 8 different languages with highest publication in English language (765, 96%) followed by French (12, 1.51%), Japanese (6, 0.76%), Portuguese (4, 0.50%), Chinese (2, 0.25%), German (2, 0.25%), Italian (1, 0.13%) and Spanish (1, 0.13) Fig. (1B).

### Journals

Analysis of source titles for quassinoid publications revealed that these articles were published in 257 journals. The most productive journals are phytochemistry with 56 publications followed by the journal of natural products (51 publications), journal of organic chemistry (43), tetrahedron letters (37 publications), planta medica (26 publications). The top 10 journals with an impact factor (JCR 2018) are listed in Table 2. Journal of American chemical society is the journal with the highest impact factor, *i.e.* 14.695, which published 15 papers on quassinoids. There are 152 source titles that published only 1 publication, 45 journals with 2 publications each, 20 journals with 3 publications each, and 9 journals with 4 publications.

### Authors

The list of top 10 authors in quassinoids literature are shown in Table 3. The 793 publications were written by 2298 authors either individually or in collaboration. Kuo-Hsiung, Lee from the University

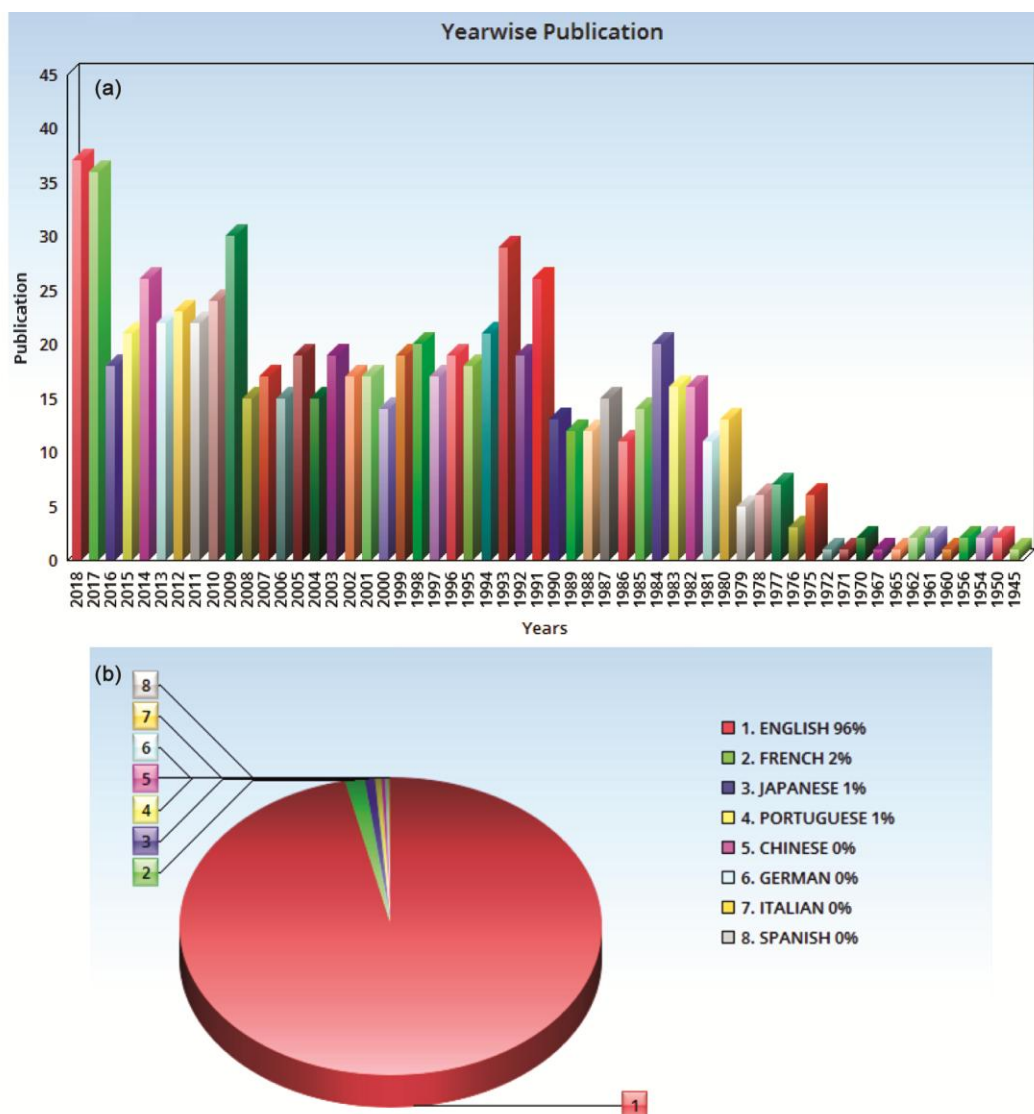


Fig. 1 — (A) Year– wise publications and (B) Language by the distribution of papers in the quassinoids research

Table 1 — Authorship pattern and document types of the quassinoids research determined from the WOS publications

Authorship pattern	Publications	Document Types	Records
Single Author	24	Article	651
Two Author	135	Note	48
three Author	108	Review	45
Four Author	144	Meeting Abstract	21
Five Author	122	Proceedings Paper	17
Six author	95	Letter	15
Seven Author	57	Editorial Material	2
Eight Author	48	—	—
Nine Author	24	—	—
>=10 Author	16	—	—

of North Carolina, USA is leading the list of authors with 39 publications having 1387 citations followed by P A Grieco of Montana State University, the USA with 38 publications and 831 citations. M Okano of Hiroshima University, Japan with 36 publications and 758 citations. K L Chan of University Sains Malaysia and M Fukmiya of Hiroshima University, Japan has 32 publications each with 610 and 611 citations respectively. Among the top 10 authors four authors are from Japan, two authors from the USA and England each and one author from Malaysia and France. Based on citations received K H Lee is the most cited author followed by J D Phillipson, and D C Warhurst form the University of London,

Table 2 — Top 10 Journals on quassinoids research

Sl. No	Journal	Impact Factor (JCR 2018)	Publication	Citations (upto 2018)
1	Phytochemistry	2.905	59	1024
2	Journal of Natural Products	4.257	51	1410
3	Journal of Organic Chemistry	4.745	43	1612
4	Tetrahedron Letters	2.259	37	592
5	Planta Medica	2.746	26	844
6	Chemical & Pharmaceutical Bulletin	1.405	23	460
7	Journal of Ethnopharmacology	3.414	22	861
8	Tetrahedron	2.379	17	298
9	Phytotherapy Research	3.766	17	469
10	Journal of The American Chemical Society	14.695	15	656

Table 3 — Productive Authors and affiliation in Quassinoids publication

Sl. No	Author	Organization	Publication	Citation
1	Lee, Kuo-Hsiung	Univ N Carolina, USA	39	1387
2	Grieco, P A	Montana State Univ, USA.	38	831
3	okano, M	Hiroshima Univ, Japan.	36	758
4	Chan, K L	Univ Sains Malaysia, Malaysia.	32	610
5	Fukmiya N	Hiroshima Univ, Japan.	32	611
6	Polonsky J	Inst Chim Subst Nat, France.	30	640
7	Phillipson, J D	Univ London, England.	24	1341
8	Koike K	Toho Univ, Japan.	24	386
9	Tagahara, K	Kobe Pharmaceutical University, Japan	23	443
10	Warhust D C	Univ London, England.	21	1111

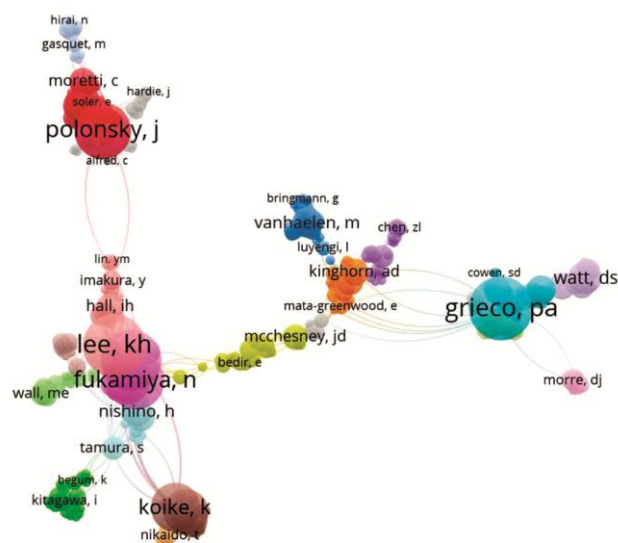


Fig. 2 — Authors collaboration network

the UK with 1341 and 1111 citations, respectively. The collaboration network among authors is shown in Fig. 2. K H Lee with 200 link strength showed the highest link strength followed by M Okano with 179, N Fukamiya with 160 link strength, K Tagahara with 121 link strength.

#### Organizations

There are more than 500 organizations that contributed to quassinoids research in the epoch. In

Table 4 — Top 10 Organizations in Quassinoids publication

Sl. No	Organization	Publication	Citation	Avg. Citation
1	Univ Sains Malaysia	55	1029	18.71
2	University of North Carolina	43	1507	35.05
3	CNRS	36	668	18.56
4	Hiroshima University	36	748	20.78
5	Indiana University	36	856	23.78
6	Univ of London	31	1741	56.16
7	Univ Paris Scalay	27	526	19.48
8	Kobe Pharmaceutical University	26	484	18.62
9	London School of Hygiene Tropical Medicine	24	1209	50.38
10	Toho University	24	373	15.54

terms of the number of publications, University Sains Malaysia, Malaysia is the top organization with 55 publications *i.e.*, approx 7.0% of the total publication followed by the University of North Carolina, USA (43), CNRS, Hiroshima University, Japan, and Indiana University, the USA with 36 publications each. As given in Table 4, based on citations received from the University of London, the UK is the most cited organizations with 1741 citations followed by the University of North Carolina, USA (1507), London School of Hygiene and Tropical

medicine, UK (1209), and University Sains Malaysia, Malaysia with 1029 citations.

**Countries**

The country-wise analysis of 793 publications reveals that there are 72 countries. The highest number of publications was from the USA with 208 publications followed by Japan with 147 publications, The Peoples Republic of China with 83 publications, Malaysia with 80 publications, and England with 51 publications. The list of top 15 countries with publication and its corresponding citations on quassinoids is shown in Fig. 3. There are 24 countries with solitary publications, 6 number of countries with two publications each, and 10 countries with 3 publications each. The clustering of countries on the basis of co-citations among countries is shown in Fig. 3.

**Keywords**

Analysis of keywords reflects that there were a total of 1218 author keywords used by authors (Fig. 4A). The most frequent keyword is Simaroubaceae with 115 occurrences, followed by quassinoids by 113 occurrences and quassinoid by

63 occurrences, and *Eurycoma longifolia* with 51 occurrences. There are 16 keywords with more than 10 occurrences and 995 keywords with a single occurrence. The clusters of keywords plus assigned by WOS for indexing are reflected in Fig. (4A). Analysis of the title and significant abstract terms were also done by using VOSViewer.

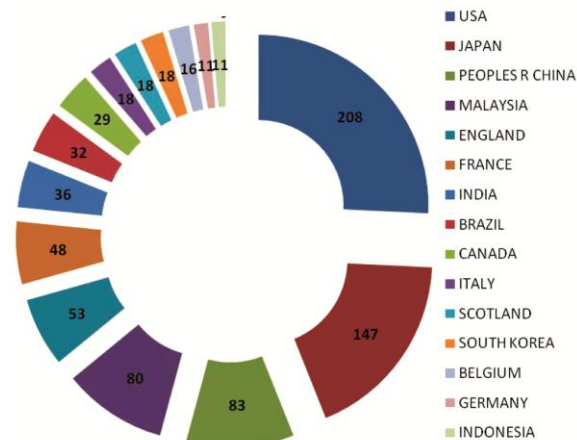


Fig. 3 — Country wise publication share

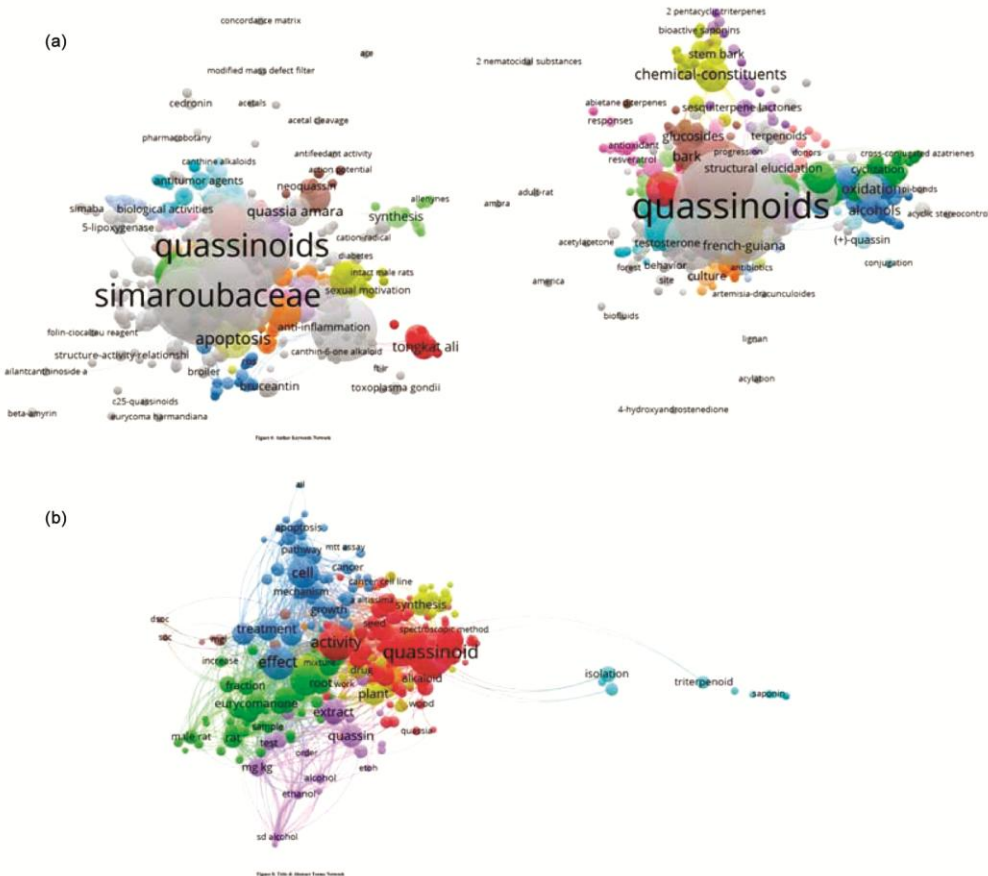


Fig. 4 — A network of quassinoids research (A) Keywords plus (B) Relevant Terms

Table 5 — Top 10 highly cited publications in Quassinoids research

Sl. No	No of Citations	Author(s)	Title	Journal	Doc. Type	Year
1	376	Chitwood D J	Phytochemical based strategies nor nematode control	Annual Review of Phytopathology	Review	2002
2	327	Solis P N, Wright C W, Anderson M M, Gupta M P, Phillipson J D	A microwell cytotoxicity assay using <i>Artemia-salina</i> (Brine Shrimp)	Planta Medica	Article	1993
3	322	Kraus Ga, Taschner M J	Model studies for the synthesis of quassinoids .1. construction of the bce ring-system	Journal of Organic Chemistry	Letter	1980
4	223	Kaur K, Jain M, Kaur T, Jain R	Antimalarials from nature	Bioorganic & Medicinal Chemistry	Review	2009
5	199	Kupchan S M, Britton RW, Lacadie J A, Ziegler M F, Sigel C W	Isolation and structural elucidation of bruceantin and bruceantinol, new potent antileukemic quassinoids from brucea-antidysenterica	Journal of Organic Chemistry	Article	1975
6	169	Lee K H	Discovery and development of natural product-derived chemotherapeutic agents based on a medicinal chemistry approach	Journal of Natural Products	Review	2010
7	152	Wright C W, Oneill M J, Phillipson J D, Warhurst D C	Use of microdilution to assess <i>invitro</i> antiamoebic activities of brucea-javanica fruits, simarouba-amara stem, and a number of quassinoids	Antimicrobial Agents And Chemotherapy	Article	1988
8	145	Brummond K M, Chen H F, Sill P, You L F	A rhodium(i)-catalyzed formal allenic alder ene reaction for the rapid and stereoselective assembly of cross-conjugated trienes	Journal of The American Chemical Society	Article	2002
9	125	Kardono L B S, Angerhofer C K, Tsauri S, Padmawinata K, Pezzuto J M, Kinghorn A D	Studies on indonesian medicinal-plants .4. cytotoxic and antimalarial constituents of the roots of eurycoma-longifolia	Journal of Natural Products	Article	1991
10	121	Lee K H	Novel antitumor agents from higher plants	Medicinal Research Reviews	Article	1999

There were total of 10018 terms retrieved after analysis of relevant terms. The clustering of title and abstract terms with quassinoids, the most used terms in title and abstract are shown in Fig. (4B). There are 10 terms with more than 100 occurrences with quassinoids the most frequent term with 446 occurrences followed by compound (274), structure (164), study (130). As many as 7150 terms have single occurrences, 1324 terms have appeared two times, and 493 terms appeared thrice in quassinoid publications.

#### Highly Cited Publications

The top 10 cited publications on quassinoids highlights in Table 5. The most cited work is a review authored by DJ Chitwood entitled “Phytochemical based strategies for nematode control” published in *Annual Review of Phytopathology* in year 2002 cited 376 times, followed by Solis *et al.* published in *Planta medica* in year 1993 having title A Microwell

Cytotoxicity Assay Using *Artemia-Salina* (Brine Shrimp) with 327 citations. Of 10 highly cited publications, 6 are research articles, 3 are Reviews, and 1 is Letter. These 10 articles have been published in 10 different journals.

#### Conclusions

The present study confirms that research on quassinoids has increased in recent years as evident by publications output, but researchers need to work on clinical trials of isolated quassinoids for its biological activity which will help in drug development. Further, collaboration on quassinoids also needs to boost up for quality results. If reported biologically active properties of quassinoids are converted into the development of new drugs to fight HIV, Cancer, and many other life-threatening diseases, it will be a boon to mankind and pharmaceuticals.

Thus, in this article, we examined the worldwide literature found in SCI- E journals of up to 2018 on quassinoids that is a triterpenoid pure group of ingredients. We've also analyzed the year wise publication development, most prolific writers, countries and organizations, most prolific journals, frequencies of search phrases, and appropriate terms included in title, abstract and keywords. The authorship pattern and also collaboration network between nations, languages, and authors of publication also have been examined. In general, this particular compilation is going to help as a crucial aid to relate to the comprehensive proof about the quassinoids research

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