Research Article

Bibliometric Analysis of Marine Traditional Chinese Medicine in Pharmacopoeia of the People’s Republic of China: Development, Differences, and Trends Directions

Wenxuan Cao,1 Jia Liu,1 Yulin Dai,2 Yashuang Zhou,1 Ruili Li,3 and Peng Yu1

1Department of Pharmaceutical Science, Changchun University of Chinese Medicine, Changchun 130117, China
2Jilin Ginseng Academy, Changchun University of Chinese Medicine, Changchun, Jilin 130117, China
3Graduate School, Changchun University of Chinese Medicine, Changchun 130117, China

Correspondence should be addressed to Ruili Li; 377311060@qq.com and Peng Yu; 342905933@qq.com

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Background. Marine traditional Chinese medicine (MTCM) is a class of traditional medicine that has antitumor, anti-inflammatory, and antiviral properties. Bibliometric approaches were used in this study to conduct systematic research in order to gain a complete picture of MTCM research around the world.

Methods. CiteSpace and NoteExpress software were utilized as tools to examine the information about authors, sources, keywords, etc. Chinese publications were collected from the CNKI, VIP, and WANFANG databases; English publications were collected from the Web of Science database.

Results. A total of 10080 publications were screened, and the search volume of Chinese literature is greater than that of English literature; Nanjing University of Chinese Medicine, China, and Jeju National University, South Korea, published a greater number of articles than other institutions; the scholars Zhaohui-Zhang and Youjin-Jeon have published the highest number of articles in the world. MTCM of shells was often researched for inorganic elements, and data mining methods were applied frequently; MTCM of animals was commonly used for antifatigue and was taken authenticity identification owing to the scarcity of resources; scholars conducted the most research on MTCM of plants, this category usually for antitumor, anti-inflammatory, and antioxidant purposes, and the mechanisms of action were studied in depth. The Chinese literature has undertaken a multifaceted research study based on the theories of processing and the nature of TCM. In the English literature, in-depth studies have been done from the perspectives of the mechanism of action, the extraction and purification of active substances, etc.

Conclusions. According to the analysis of keywords, different medicinal partspresent their own special research directions, and different researchhotspotshave also emerged under different medical theories. The development of MTCM is moving in the direction of standardization and modernization, thanks to the development of cross-disciplinary research as well as the use of several new technologies and statistical techniques.

1. Introduction

The ocean accounts for more than 70% of the earth’s surface area, and it is the cradle of life and a crucial source of supplies for human nutrition. Due to the particular marine environment of high salt, high pressure, hypoxia, and lack of sunlight, marine organisms and plants often produce a range of secondary metabolites with specific activities during growth and metabolism [1–3]. For example, polysaccharides [4] or macrolides [5] from the ocean have, without a doubt, incalculable value in the medical area. According to the Pharmacopoeia of the People’s Republic of China (ChP), marine medicines can be divided into marine traditional Chinese medicines (MTCM), marine chemical medicines, and marine biological products [6]. Among them, MTCM refers to marine natural medicines used for disease prevention and health care under the guidance of traditional Chinese medicine (TCM) theory [7, 8], which include marine botanicals, marine animal medicines, and marine mineral medicines [9]. MTCM, as an important part of
traditional Chinese medicine resources, is rich in resources and unique in its therapeutic benefits; its research and development have focused widespread attention on the medical profession [10–12]. China, as the originator of TCM, has been using MTCM to treat ailments for nearly 2,000 years, and many MTCMs have been confirmed to be medically helpful through long-term clinical trials [13]. In 2012, the “Twelfth Five-year Plan” launched in China clearly put forward the requirement of “scientific planning for the development of marine economy, rational exploitation of marine resources, and focus on cultivation and growth of marine biomedicine.” Since the implementation of this plan, MTCM has become a popular research topic in the field of marine economy, and focus on cultivation and growth of marine biomedicine. Therefore, we chose 11 MTCM recorded in the 2020 version of the ChP as search subjects. All Chinese literature data for this study were obtained from the databases of the China National Knowledge Infrastructure (CNKI), Weipu (VIP), and WANFANG. English literature data were obtained from the Web of Science Core Collection (WoS). Search terms include “Marine materia medica,” “Marine traditional Chinese medicine,” “Shijueming, Marginifera Concha,” “Kunbu,” “Hippocampus,” “Zhenzhumu, Frondes Concha Cyclinae Concha,” “Haipiaoxiao,” “Sepiae Endoconcha,” “Haima, Hippocampus,” “Zhenzhhu, Marginifera Concha,” “Hailong, Synnathus,” “Haizao, Sargassum,” “Muli, Ostreae Cconcha.”

The data-duplication procedure was accomplished by using NoteExpress (v3.5.0.9054) and CiteSpace 5.7.R2’s “Data Import/Export-Remove Duplicate” function; bubble charts were plotted using https://www.bioinformatics.com.cn, a free online platform for data analysis and visualization. Figure 1 explains the entire process of the study.
different data sources. Figure 2 explains the meaning of the annual rings and the time represented by the color of the annual rings in different studies.

3. Results and Analyses

3.1. Analysis of Volume of Publication Published. Because there is so much retrieved Chinese literature, the quality is spotty, with numerous “folk recipes” and “informal prescriptions.” Except for analyzing the volume of literature published, other analytical project data were collected from the journal recorded in “Guide to Chinese Core Journals (GCCJ)” and the Chinese Journal of Marine Drugs.

3.1.1. The Relationship between the Number of Publications and Particular Year. After de-duplication, a total of 9,958 publications were collected, including 9,301 Chinese publications (1,559 publications from GCCJ) and 657 English publications. Figure 3 is the annual distribution trends of them. From the perspective of publication volume, the overall publication volume of Chinese literature is much higher than that of English literature, despite the fact that the number of publications in GCCJ is only marginally higher than that of English literature. From the perspective of the trend of publication volume, the publication volume of Chinese literature grew at a steady rate until the twenty-first century. From 2000 to 2015, the number of publications rose sharply, followed by a sharp fall, whereas the number of publications in the GCCJ has remained stable since the beginning of the twenty-first century, with no precipitous fluctuations. From 1980 to 2013, the volume of English literature progressively increased, remained steady in 2013, however, and increased dramatically in 2018, with the annual volume of literature surpassing that of the GCCJ.

As previously stated, the rapid development of the contemporary nautical and fishing industries has enabled people to better understand the sea. Due to the special growth environment of MTCM, the exploration of marine areas in China may have hit a snag since 2010. In comparison to Chinese literature, English literature is still in a phase of steady productivity, with more publications than GCCJ literature.

3.1.2. Number of Publications per MTCM. Information from Chinese and English literature was unified and summarized in NoteExpress software. We counted the amount of literature obtained for each search term separately and summarized it in WPS software before creating a double-column chart, and the results are shown in Figure 4. The search item “Ostreae Concha” had the largest number of publications in the Chinese literature, and it was also the most regularly prescribed in MTCM prescriptions [33]. The article “From the usefulness and utilization of Ostreae Concha to the
substitution of Ostreae Concha for keel bones,” published by Pei in the Journal of traditional Chinese medicine served as the research starting point for Ostreae Concha. The major concentration of research in Chinese literature is on shell and botanical-based TCM; animal-based TCM such as “Hippocampus” and “Syngnathus” has received less attention because of a lack of resources and high prices. The chart’s most striking result in English literature is that the search term “Sargassum” (707) is higher than others. The experimental literature “Antibiotic characteristics of Sargassum natans from Puerto Rico,” published in the Journal of Pharmaceutical Sciences in 1961, was the starting point for the English literature investigation [34].

3.2. Cooperation Analysis of Research Countries, Authors, and Institutions. To obtain a cooperation atlas and bubble chart, the network node was set to “country” (Figure 5); take note that the source of the data here is from WoS. The number of publications is the highest in China (197), followed by South Korea (115), India (69), and Japan (57), all of which have more than 50 publications. The centrality of China reached 0.55, indicating that China is an important location for information transfer in the field of MTCM research.

We set the network node to “institution” and then filtered, merged, and renamed all institutions into first-class institutions and visualized the data results as shown in Figure 6. Nanjing University of Chinese Medicine, China
(NJUCM) (51), and Jeju National University, South Korea (JEJUNU) (38), ranked first in the number of English and Chinese publications, respectively. Chinese institutions can be split into two categories: Chinese medical related universities and “marine” related universities. It is noteworthy that Ocean University of China, China (OUC), and the Chinese Academy of Sciences (The Institute of Oceanology), China (CASIO), have published numerous papers in both language journals. The centrality of NJUCM and Chonnam National University (CNU), South Korea, is all over 0.1, indicating that they are major communication nodes and have scientific authority in the field. In addition

Figure 4: Statistics about the number of publications on 11 MTCM. SYN. = Syngnathus; SEP. = Sepiae Endoconcha; SAR. = Sargassum; OST. = Ostrea Concha; MER. = Meretrix Concha Cyclinae Concha; MAR.C. = Margaritifera Concha; MAR. = Margarita; LAM. = Laminariae Thallus Eckloniae Thallus; HIP. = Hippocampus; HAL. = Halotidis Concha; ARC. = Arcae Concha; positioned at lines 174–188.

Figure 5: Countries’ cooperation atlas and bubble chart based on the English literature. (a) Cooperative atlas of countries. (b) Bubble chart of the countries’ characteristics based on the research data obtained from the English literature (top 10); positioned at lines 195–200.
to these two institutions, the Egyptian Knowledge Bank (EKB) in Egypt, the University of Toyama in Japan, and Alagappa University in India were active in this field; these results matched the country analysis above. In Chinese literature, CASIO and OUC frequently appear, while other higher education institutions generally collaborate with their affiliates and clinical hospitals. Compared to institutions in Chinese literature, institutions in English literature cooperate more closely. Taken together, the MTCM area is centered on Chinese institutions led by NJUCM and South Korean institutions led by JEJUNU, all of which have professional teams and established research processes, as well as a wealth of expertise and excellent research skills.

As indicated in Figure 7, Chinese scholar Zhaohui-Zhang is the author with the most publications (25) in Chinese literature and routinely collaborates on Hippocampus and Syngnathus research with Zhang et al. [35–37]. Changyun-Wang (22) is a professor at OUC; he conducted some research studies on the characterization and microscopic identification of TCM [38] as well as the activity or structure of marine fungi [39, 40]. Youjin-Jeon, a South Korean scholar with the highest number of publications (30), is a professor at the College of Marine Biomedical Sciences, JEJUNU. He collaborated with Ginnae-Ahn and Fernando-Ilekuttige Priyan Shanura. [41, 42]. Chao-Li, a young professor at the South China University of Technology (SCUT), is the third person to publish the most English literature. He has worked with Xiong-Fu, Qiang-Huang, and Lianghuang-Cao on a number of occasions and conducted research studies on both sea cucumbers and Sargassum [43, 44]. Only Gansheng-Zhong’s centrality reaches 0.1, as depicted in Figure 7(c), indicating that he was serving as a connector between authors.

To summarize, despite the fact that China is the source of MTCM with a significant number of publications, the collaboration network density of authors in English literature was higher than that of authors in Chinese literature. This finding is consistent with the previous findings on institutions.

3.3. Analysis of Journals. The top 10 lists of published journals in Chinese and English were obtained by using the “data analysis” function of NoteExpress (Tables 1 and 2). The most published Chinese journal is the Journal of Traditional Chinese Medicine (156), which was founded in 1955. The second place is the Chinese Journal of Marine Drugs (124), which is the first worldwide academic journal devoted to marine medicine; however, it has a somewhat lower compound impact in comparison. The Chinese journals studying MTCM, whose research areas focus on Chinese medicine, TCM, and pharmacology, are covered. The English journal with the highest number of publications is Marine Drugs (95), which was established at OUC and whose founding editor-in-chief is the professor Huashi-Guan. The overall quality of articles published in English journals is strong, and numerous high-level journals, such as Carbohydrate Polymer Technologies and Applications, are included in JCR Q1. The English literature consisted of approximately 200 periodicals focused on medicine, molecular biology, chemistry, fisheries, and other fields.
Figure 7: Author cooperation atlases and bubble charts based on the English and Chinese literature. (a) Cooperation atlas of authors who have published the Chinese literature. (b) Cooperation atlas of authors who have published the Chinese literature. (c) Bubble chart of the author characteristics for the research data obtained from the Chinese and English literature (top 10, respectively); positioned at lines 229–242.

Table 1: Top 10 published journals based on the CNKI, VIP, and WANFANG.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Journal name</th>
<th>Volume of publication</th>
<th>Compound IF (2021)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Journal of Traditional Chinese Medicine</td>
<td>156</td>
<td>2.313</td>
</tr>
<tr>
<td>2</td>
<td>Chinese Journal of Marine Drugs</td>
<td>124</td>
<td>0.669</td>
</tr>
<tr>
<td>3</td>
<td>Lishizhen Medicine and Materia Medica Research</td>
<td>115</td>
<td>1.136</td>
</tr>
<tr>
<td>4</td>
<td>China Journal of Chinese Materia Medica</td>
<td>108</td>
<td>3.076</td>
</tr>
<tr>
<td>5</td>
<td>Journal of Chinese Medicinal Materials</td>
<td>101</td>
<td>1.309</td>
</tr>
<tr>
<td>6</td>
<td>Chinese Traditional Patent Medicine</td>
<td>98</td>
<td>1.668</td>
</tr>
<tr>
<td>7</td>
<td>Chinese Traditional and Herbal Drugs</td>
<td>89</td>
<td>3.16</td>
</tr>
<tr>
<td>8</td>
<td>Chinese Journal of Experimental Traditional Medical Formulae</td>
<td>61</td>
<td>3.038</td>
</tr>
<tr>
<td>9</td>
<td>China Journal of Traditional Chinese Medicine and Pharmacy</td>
<td>41</td>
<td>2.083</td>
</tr>
<tr>
<td>10</td>
<td>Journal of Basic Chinese Medicine</td>
<td>35</td>
<td>1.204</td>
</tr>
</tbody>
</table>

Table 2: Top 10 published journals based on the WoS.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Journal name</th>
<th>Volume of publication</th>
<th>IF (2021–2022)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Marine Drugs</td>
<td>95</td>
<td>6.085</td>
</tr>
<tr>
<td>2</td>
<td>International Journal of Biological Macromolecules</td>
<td>84</td>
<td>8.025</td>
</tr>
<tr>
<td>3</td>
<td>Carbohydrate Polymer Technologies and Applications</td>
<td>46</td>
<td>10.723</td>
</tr>
<tr>
<td>4</td>
<td>Food Chemistry</td>
<td>21</td>
<td>4.004</td>
</tr>
<tr>
<td>5</td>
<td>Journal of Agricultural and Food Chemistry</td>
<td>21</td>
<td>9.31</td>
</tr>
<tr>
<td>6</td>
<td>Phytochemistry</td>
<td>20</td>
<td>5.895</td>
</tr>
<tr>
<td>7</td>
<td>Molecules</td>
<td>17</td>
<td>4.927</td>
</tr>
<tr>
<td>8</td>
<td>Food &amp; Function</td>
<td>16</td>
<td>6.317</td>
</tr>
<tr>
<td>9</td>
<td>Natural Product Research</td>
<td>14</td>
<td>2.488</td>
</tr>
<tr>
<td>10</td>
<td>Chemistry of Natural Compounds</td>
<td>13</td>
<td>0.830</td>
</tr>
</tbody>
</table>
3.4. Analysis of Keywords

3.4.1. Cooccurrence Analysis of Keywords. A keyword is a succinct expression of an article’s fundamental substance, and to a certain extent, the high frequency of a term at a given time reflects the period’s research hotspots [45]. Because different medicinal portions of the MTCM are utilized for different purposes and ways [46], we have therefore categorized the MTCM into 5 categories based on the sections of the medicine used [47] (according to 3.1.2, the keyword analysis of the English literature was limited to the category of plant because the search results of the English literature almost entirely circled around Sargassum):

(i) Category 1: Shell: Haliotidis Concha, Arcae Concha, Margaritifera Concha, Meretricis Concha Cyclinae Concha, Ostreae Concha

(ii) Category 2: Animal’s whole body: Hippocampus, Syngnathus

(iii) Category 3: Animals’ endoskeleton: Sepiae Endoconcha

(iv) Category 4: Animal’s secretions: Margarita

(v) Category 5: Plant: Sargassum, Laminariae Tallus, Eckloniae Tallus

Figure 8 depicts the difference in the number of publications between the result of 3.1.2 and this result: the previously counted ranking list shows Ostreae Concha at the top; however, this statistic shows Haliotidis Concha at the top. As a result of this finding, we can deduce that an additional high-quality study on Haliotidis Concha has been undertaken. This TCM has a long history of use, and it was commonly pulverized and powdered to cure eye diseases [48]. Furthermore, it was often used to treat vertigo by Mr. Bohua-Kong, a famous old Chinese medicine practitioner [49]. Ma et al. [50] discovered that aqueous extracts of Haliotidis Concha can also decrease angiotensin-converting enzyme (ACE) activity and have a powerful and long-lasting antihypertensive impact. We can see that “data mining,” “determination of inorganic elements,” and “famous doctor’s experience” are all prominent by observing the statistics on quantity and centrality in Figure 8(b). Due to the fact that calcium salts and microelements are the key chemical components of shellfish class MTCM, their contents are closely associated with the efficacy and quality of MTCM, and their contents are also closely tied to the origin, growing period, and marine biological environment [51, 52]. Beyond that, the combination of data mining and association rules is a novel technique to summarize and explore the medication rules of famous Chinese medicine practitioners.

Figure 9 contains the keywords (category 2) cooccurrence atlas. Apart from the species nouns of Hippocampus and Syngnathus, the keyword “fatty acids” has a higher centrality than others. Both the Hippocampus and the Syngnathus contain 14 different types of fatty acids [53], particularly the unsaturated fatty acids ARA, EPA, and DHA, which are essential nutrients the human body cannot produce on its own [54, 55]. They play a significant role in maintaining body health and curing ailments, and their contents are frequently employed as a quality evaluation index [56]. In terms of pharmaceutical effects, “antifatigue” appears in the cooccurrence atlas, and research has verified that both the Hippocampus and the Syngnathus have antifatigue properties [57, 58]. Apart from these, “morphological identification” and “molecule identification,” both part of the identification process, indicate that scholars have conducted some discriminating research in this field.

The keyword analysis result for category 3 is similar to that of category 1. Scholars often apply data mining methods and regard inorganic elements as research objects. Funnily enough, the keyword “polysaccharide” appears prominently
Although Sepiae Endoconcha is an animal bone, it also contains substances such as mucus, polysaccharides, and enzymes [59]. Sepiae Endoconcha polysaccharide (CPS-1) has been proven in studies to speed up the healing and repair of ulcer tissue as well as have a cytoprotective effect on the stomach mucosa [60, 61].

Margarita is generated in the body by stimulation of bivalves as described in Chp [62], so we classify it in the animal secretion class MTCM. By observing Figure 11, scholars generally conducted research on Chinese patent medicines containing Margarita (e.g., Liushen Pill, Zhenzhu Powder), and it was often detected by chromatography (e.g., TLC, HPLC, or GC) [63, 64].

Figure 12 displays the keywords characteristics of category 5 in Chinese and English literature. The beginning of Sargassum research in China has emphases on its active ingredients (e.g., polysaccharides, sodium alginate [65]) and their effects while combined with other TCM (e.g., Laminariae Thallus Eckloniae Thallus, Glycyrrhizae Radix Et Rhizoma [66, 67]). Researchers have also looked into the extraction and pharmacological activity of polyphenolic compounds. In English literature, there is a substantial amount of research on fucoidan and seaweed polysaccharides. The high frequency keyword count of the passages showed that most of the English literature is based on cell research in vitro and rat experiments in vivo to verify its antitumor, anti-inflammatory, antioxidant, and other effects [68–70]. Figure 12(c) illustrated the disparities in the prominence between Chinese and English literature. The results of keyword analysis in Chinese literature, such as “Sargassum,” “Laminariae Thallus Eckloniae Thallus,” and “eighteen-clashes,” show that the centrality of these words is over 0.1. The majority of English literature keywords have a centrality of 0.03–0.08, with the centralities of “purification” and “algae” being greater than or equal to 0.1. This result indicated that the authors of the English literature have made a thorough study of Sargassum from every viewpoint, and the researchers have spent some time thinking about the extraction and purification processes.

3.4.2. Cluster Analysis of Keywords. Each category of keywords was administered to clustered analysis independently after being calculated by the LLR clustering algorithm, as illustrated in Figure 13, and the characteristics of each cluster are presented in Tables 3–8.

3.5. Analysis of Trends

3.5.1. Burstiness Analysis of Countries, Authors, and Institutions. Five burstiness atlases were collected after applying the burstiness function (Figure 14). In Figure 14(a), Japan has the highest prominence value (14.17), followed by South Korea (6.25), but Malaysia and India were still in the emergence time range until 2020, which indicated that they were experiencing a research boom. Figures 14(b) and 14(c) display the statistics for institutions. The prominence value of Guangxi University of Chinese Medicine (GXTCMU) (7.59) is higher; this institution has seen a boom in publication since 2016 and keeping highly product. OUC is listed in both statistics atlases, and Chengdu University of Traditional Chinese Medicine (5.35), Shandong University of Traditional Chinese Medicine (5.1), CUN (4.98) and SCUT (4.69) also have high prominence values and have conducted research in this field recently. In the burstiness atlases of authors (Figures 14(d) and 14(e)), Zhaohui-Zhang (5.52), and Luoshan-Xu (5.52) have the highest prominence value. They are not affiliated with the same institution but
collaborate closely to do research on *Hippocampus* and *Syngnathus*. Chen et al. also have a high prominence value (5.04), they are in the same research team with Erwei-Hao at GXTCMU. This conclusion substantially confirmed the findings in Figure 14(b), and research progress and safety evaluation of MTCM are part of their research [71]. You-jin Jeon is an author in English literature with the highest number of publications and the largest prominence value (6.34). Xiong-Fu (3.43) and Chao-Li (3.43), who work at SCUT, although both of them do not have high prominence value, there is no denying that their contributions have enhanced the prominence value of their institution, and they have been active in recent years.

### 3.5.2. Leapfrog Analyses of Keywords

Keyword leapfrog atlases were obtained by setting the presentation to "Timezone View" (Figures 15–19).

Figure 15 shows that *Haliotidis Concha* and *Margaritifera Concha* appeared earlier. MTCM research on shellfish class was limited to a single TCM from 1950 to 1980, and researchers began to explore ingredients in 1980. The emergence of the keywords "data mining" and "association rules" around 2010 suggests that the application of various algorithms to explore medication rules became common.

The starting point of the node leap is presented in Figure 16. After 1980, scholars conducted some research on the antifatigue effect of *Hippocampus* and *Syngnathus*...
around 1990, then they began to study the therapeutic impact of “warming the kidney to invigorate yang” until 1995. Fatty acids have been studied for longer and in greater depth, whereas amino acids have only recently been investigated. After 2015, due to the paucity of Hippocampus, research on morphological identification, molecular identification and origin has sprung up.

By observing the leapfrog atlas (Figure 17), the research on animal’s endoskeleton class (*Sepiae Endoconcha*) MTCM was also started earlier, and the research on it was relatively single until 1980. Microelements, calcium carbonate, and amino acids have been researched since 1980, while polysaccharide components have been researched since 2000. Similarly, around 2010, research on data mining emerged.

The leapfrog atlas of animals’ secretion class MTCM (Figure 18) displays fewer keywords; the result is organized into three periods depending on research feature. Early stage (before 2000): pharmacological effects or clinical observation studies on *Margarita*-containing TCM compounds. Mid-term (2000–2010): application of chromatography technologies for chemical composition detection or quality control. Later stage (after 2010): analysis of pharmaceutical rules and determination of amino acid content in *Margarita* using various algorithms.

As illustrated in Figure 19, there are some variations between the Chinese and English literature on the research points and timing of plant class MTCM. A hiatus in Chinese literature research on plant class MTCM existed from 1950–1990, and along with the increased attention to *Sargassum* worldwide, Chinese researchers made a qualitative and quantitative jump in their research on *Sargassum* starting in 1990. Prior to 2000, the research in China was limited to the efficacy of crude extracts, and after 2000, studies on the mechanism of action were carried out successively. Earlier studies in English literature had deeply studied polysaccharides and fucoidan for extended periods of time, revealing antitumor, antioxidant, anti-inflammation, and other effects. Until 2010, its modulatory function on the immune system and anticoagulant effects were also excavated. Since 2015, scholars have started to investigate at the molecular structural characterization level and spare no effort to optimize the extraction procedures.

4. Discussion

This study applied CiteSpace 5.7.R2 software from the perspectives of publication number, author, institution, and keyword to research and summarize the publication situation, country-author-institution cooperation, research path evolution, and key research directions of China and other countries’ research in the field of MTCM.

Through the analysis of the cooperation between countries, it is obvious that China was widely recognized by international peer researchers for producing high-quality and co-cited literature. South Korea, India, and Japan are all coastal countries with favorable geographic conditions and abundant natural resources. Especially in South Korea, where the aquatic industry is well developed, this condition...
provides a strong technological foundation for the burgeoning businesses of marine medicine and healthy food [72].

The cooccurrence analyses of institutions and authors showed that institutions in China and South Korea outperformed those in other countries, but the lower density of collaboration in China is a lateral expression of a lack of communication between institutions. This can be classified for two reasons: first, Chinese academics tend to conduct research from a theoretical standpoint, yet relevant records are scarce and vague, which makes research more challenging. Second, there is a big fraction of Sargassum-related topics in English literature, which is the most important reason for the high density of collaboration. To balance this situation, the Chinese government, research institutions, and scholars could consider the following perspectives.
We have three recommendations for the related departments. First of all, now that only 11 MTCM are recorded in the ChP, associated departments should strengthen the resource census and thoroughly investigate the resource base, thereby boosting more research-worthy MTCM incorporated into the ChP, such as sea cucumbers, sea urchins, and sea stars, which have established mature research systems is necessary.

Secondly, through keyword cooccurrence analyses, we found the resources of some species are being depleted; for example, *Hippocampus* is currently in serious decline and has suffered depletion of its natural resources; it is now listed on the IUCN Red List and the China species Red List [73]. Hence, it is imperative to avoid the circulation of pseudo-mixed products in the market through morphological identification, molecular identification, and content determination. Scarce resources, such as *Hippocampus* and *Syngnathus*, should be cultured in captivity or introduced as new species, prevention of species mixing, stopping counterfeit and substandard medicines to affect the effectiveness and safety of clinical use of MTCM. Finally, establishing quality standards and clinical application guidelines through qualitative and quantitative analysis of a component of MTCM, which is common in our summarized study. We found that the quality standard of MTCM is uneven, small amount of them have an easy physical or chemical identification standard and few of them have a content determination, even five different shellfish MTCM but using the same calcium carbonate content determination standard [52]. Therefore, related departments should designate a development strategy for MTCM and establish a standardized technical system.

### Table 4: Cluster information about animal’s whole body class MTCM based on Chinese literature.

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Cluster name</th>
<th>Size</th>
<th>Silhouette</th>
<th>Mean (year)</th>
<th>Top terms (LLR, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td><em>Hippocampus</em></td>
<td>24</td>
<td>0.918</td>
<td>2008</td>
<td><em>Hippocampus</em>: kidney yang deficiency, etc.</td>
</tr>
<tr>
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<td><em>Hippocampus japonicus Kaup</em></td>
<td>23</td>
<td>0.83</td>
<td>2008</td>
<td><em>Hippocampus kudaBleeker</em>: morphological identification, etc.</td>
</tr>
<tr>
<td>2</td>
<td><em>Syngnathus</em></td>
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<td>0.892</td>
<td>2005</td>
<td><em>Syngnathus</em>: clinical observation etc.</td>
</tr>
<tr>
<td>3</td>
<td><em>Syngnathus australis</em></td>
<td>20</td>
<td>0.918</td>
<td>1997</td>
<td><em>Syngnathus australis</em>: fatty acid, etc.</td>
</tr>
<tr>
<td>4</td>
<td>Pharmacological effect</td>
<td>18</td>
<td>0.826</td>
<td>2002</td>
<td>Chemical composition, hippocampus capsule, etc.</td>
</tr>
</tbody>
</table>

### Table 5: Cluster information about animal’s endoskeleton class MTCM based on Chinese literature.

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Cluster name</th>
<th>Size</th>
<th>Silhouette</th>
<th>Mean (year)</th>
<th>Top terms (LLR, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td><em>Sepiae Endoconcha</em></td>
<td>43</td>
<td>0.99</td>
<td>2004</td>
<td><em>Sepiae Endoconcha</em>: adsorption, etc.</td>
</tr>
<tr>
<td>1</td>
<td>Clinical experience</td>
<td>19</td>
<td>0.999</td>
<td>2010</td>
<td>Clinical experience; logistic regression, etc.</td>
</tr>
<tr>
<td>2</td>
<td>Calcium carbonate</td>
<td>13</td>
<td>0.978</td>
<td>2002</td>
<td>Chinese medicine treatment; biominerals, etc.</td>
</tr>
<tr>
<td>3</td>
<td>Polysaccharide</td>
<td>12</td>
<td>0.965</td>
<td>2010</td>
<td>Polysaccharide; biological activity, etc.</td>
</tr>
<tr>
<td>4</td>
<td>Reasonable compatibility</td>
<td>10</td>
<td>0.965</td>
<td>2010</td>
<td>Reasonable compatibility; endomycin, etc.</td>
</tr>
</tbody>
</table>

### Table 6: Cluster information about animal’s secretion class MTCM based on Chinese literature.

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Cluster name</th>
<th>Size</th>
<th>Silhouette</th>
<th>Mean (year)</th>
<th>Top terms (LLR, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Margarita</td>
<td>20</td>
<td>0.998</td>
<td>2001</td>
<td><em>Margarita</em>: toxicology, etc.</td>
</tr>
<tr>
<td>1</td>
<td>Medication rule</td>
<td>16</td>
<td>0.96</td>
<td>2017</td>
<td>Medication rule; visual fatigue, etc.</td>
</tr>
<tr>
<td>2</td>
<td>Thermogravimetric analysis</td>
<td>15</td>
<td>0.961</td>
<td>2002</td>
<td>X-ray diffraction; quality analysis, etc.</td>
</tr>
</tbody>
</table>

### Table 7: Cluster information about plant class MTCM based on Chinese literature.

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Cluster name</th>
<th>Size</th>
<th>Silhouette</th>
<th>Mean (year)</th>
<th>Top terms (LLR, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td><em>Sargassum</em></td>
<td>38</td>
<td>0.938</td>
<td>2003</td>
<td><em>Glycyrrhiza Radix et Rhizoma</em>: <em>Sargassum</em>, etc.</td>
</tr>
<tr>
<td>1</td>
<td>Sodium alginate</td>
<td>25</td>
<td>0.844</td>
<td>2007</td>
<td>Sodium alginate; microcapsules, etc.</td>
</tr>
<tr>
<td>2</td>
<td><em>Laminariae Thalassae Thalassa</em></td>
<td>25</td>
<td>0.985</td>
<td>2004</td>
<td><em>Laminariae Thalassae Thalassa</em>: laminarin, etc.</td>
</tr>
<tr>
<td>3</td>
<td>Extraction</td>
<td>24</td>
<td>0.857</td>
<td>1995</td>
<td>Extraction; purification, etc.</td>
</tr>
<tr>
<td>4</td>
<td>Biological activity</td>
<td>18</td>
<td>0.955</td>
<td>1993</td>
<td>Biological activity; phlorotannins, etc.</td>
</tr>
</tbody>
</table>

### Table 8: Cluster information about plant class MTCM based on English literature.

<table>
<thead>
<tr>
<th>Cluster ID</th>
<th>Cluster name</th>
<th>Size</th>
<th>Silhouette</th>
<th>Mean (year)</th>
<th>Top terms (LLR, p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Polysaccharide</td>
<td>73</td>
<td>0.743</td>
<td>207</td>
<td>Polysaccharide; structure, etc.</td>
</tr>
<tr>
<td>1</td>
<td>Sulfated polysaccharide</td>
<td>47</td>
<td>0.665</td>
<td>2012</td>
<td>Sulfated polysaccharide; anti-inflammatory, etc.</td>
</tr>
<tr>
<td>2</td>
<td>Biosorption</td>
<td>44</td>
<td>0.832</td>
<td>2005</td>
<td>Biosorption; alginate, etc.</td>
</tr>
<tr>
<td>3</td>
<td><em>Sargassum thunbergii</em></td>
<td>39</td>
<td>0.813</td>
<td>2006</td>
<td><em>Sargassum thunbergii</em>: <em>Endophytic fungus</em>, etc.</td>
</tr>
<tr>
<td>4</td>
<td>Ftr</td>
<td>35</td>
<td>0.832</td>
<td>2007</td>
<td>Ftr; Fick’s second law, etc.</td>
</tr>
</tbody>
</table>

As for the advice to institutions and scholars, the following perspectives can be referred to. One of them is: Chinese scholars make up the majority of the field, and they...
are particularly interested in following up on information recorded in ancient books, which is noteworthy because there is variability between the literature and ancient books about MTCM [74]. This requires the scholars to apply modern information technology to delve deeply into the literature and historical materials; “data mining” and “affiliate rules” present in our study fit with this phenomenon.

Now, only 7 MTCM have relatively complete herbal texts [35, 74–78], necessitating a thorough examination of other MTCM foundation sources. Another one is: “Theory of medicinal nature” frequently appears in our cooccurrence atlases; Chinese medicinal nature is the intrinsic characteristics that distinguish TCM from other medicines [74].

Figure 14: (a) Countries with the strongest citation bursts (top 5). (b) Institutions based on the Chinese literature with the strongest citation bursts (top 5). (c) Institutions based on the English literature with the strongest citation bursts (top 5). (d) Chinese authors with the strongest citation bursts (top 5). (e) English authors with the strongest citation bursts (top 5); positioned at lines 386–406.

Figure 15: Keyword leapfrog atlas about category 1 in Chinese literature; positioned at lines 415–419.
improve research efficiency when traditional oriental medical theory and modern western pharmaceutical theory collide.

Based on the cooccurrence, clustering, and leapfrog analyses of keywords in Chinese literature, we found MTCM has specific emphases in China, such as process methods, the medicinal nature of TCM, textual or visual identification of pseudo-mixes, etc. The processing of TCM, as a unique traditional pharmaceutical technique in China, is an essential tool and an important part of ensuring the clinical efficacy of Chinese medicine [79, 80]. When MTCM is processed, its medicinal effects, contents of some components, and medicinal properties may change [81–83]. We also concluded that scholars usually research MTCM by applying analytical tools, digging into the medication rules, and summarizing the experiences of famous doctors. After 2010, the “affiliation rules” cluster emerged, which coincides with the previous statement. Affiliation rule is a technique for mining valid relationships from huge amounts of valuable data. “Data mining” is an emerging discipline that combines theories and techniques from fields such as mathematics, statistics, and artificial intelligence. The
combination of these two has already been widely used in the TCM field [84, 85]. By classifying and analyzing the MTCM of different medicinal portions, we can see that mineral-based MTCM (shell, an animal's endoskeleton, and an animal's secretion) and inorganic elements and microelements were the focus of research; plant-based MTCM research in China concentrate on thyroid disorder or gall goiter, while research in other countries focuses on cancer or inflammation, which is another reminder of the differences between modern and traditional medicine and the need for integration. Animal-based MTCM employs the entire body of the animal as the source of medicine, and both have the pharmacological effect of “warming the kidney to invigorate yang” from a TCM perspective, while from a western medical point of view, they have an antifatigue effect.

Being different from the hotspots of research in Chinese literature, English literature focuses on *Sargassum* as a whole, preferring to explore the action mechanisms, extraction, and purification of active substances, most well studied for antioxidant and antitumor properties, but it is not limited to these two applications absolutely. Based on keywords analyses, we found that researchers often take the regulation of the signaling pathway by medicine as the starting point. Take the classical NF-κB signaling pathway as an example, inflammatory stimuli activate the NF-κB inducible transcription factor, which is found ordinarily in the cytoplasm as an inactive trimer and translocated subsequently from the cytoplasm to the nucleus, increasing the development of inflammation or cancer [86–88]. Yoon et al. [89] found that Sargachromanol G, which is isolated from the brown alga *Sargassum siliquastrum*, can inhibit the conversion of RAW 264.7 to osteoblasts by activating the NF-κB signaling pathway. By observing the keyword leapfrog and clustering analysis atlases, we have found that the technical combined application of chromatography, mass spectrometry, and spectroscopy is becoming increasingly common [90, 91]. Combining the ability of chromatography to separate complex samples with the high sensitivity of mass spectrometry or spectroscopy to determine relative molecular mass and structural information, these facilitate the investigation of the active ingredients and structures in MTCM in more depth and optimize the extraction process [92, 93].

Taken together with the discussion of keywords, it is explicit that the study of MTCM in Chinese literature started earlier while the study in English literature started later, but...
the pharmacodynamic mechanism is clearly defined. Currently, the main idea underlying MTCM applications in both Chinese and English literature is to screen medication lead compounds from marine resources, then developing and changing them structurally. Lastly, turn them into appropriate therapeutically medicines.

Based on the results of the analysis, a particularly large number of scholars have been studying *Sargassum* in recent years, in light of this, there are three proposals for subsequent scholars: first: “sulfated polysaccharide” has a prominent place in keyword analyses and it is also verified that appropriate sulphation changes have been proven to improve the biological activity of seaweed polysaccharides [94]. It has also been verified that selenium leads to some changes in the monosaccharide composition, molecular weight, and surface morphology of seaweed polysaccharides, which exhibit more pronounced inhibition of α-glucosidase activity in a noncompetitive inhibition type [95]. Continuing on from this point, scientists can consider more novel ways to modify *Sargassum* polysaccharides, which may cause unanticipated profits. Second: the optimization of extraction process is a hot research topic in recent years; however it is well known that the extraction of seaweed polysaccharides is not high and the purification process needs to be optimized [96]. So, the other components of the *Sargassum* species, such as inorganic elements and polyphenols, are likely to play a positive role. Third: MTCM is originated in China, although Chinese scholars and institutions are particularly engaged in this sector, the density of cooperation between institutions and authors is not excellent. As a result, cutting-edge institutions including NJUCM, CASIO, OUC, SCUT, etc. should make breakthroughs from the existing research base, strengthen communication and coordination, and collaborate closely to achieve more valuable and credible achievements.

Under the network mapping of the keyword analysis, we found the appearance of many disease symptoms reflected the unique activities and potential of MTCM. More than half of the MTCM have pharmacological activities such as antioxidation, antitumor and antiviral, according to researches [97]. “Antioxidation” or “oxidative stress” can be seen everywhere in the keyword analysis atasis, which show that MTCM has a most outstanding antioxidant effect. Increased oxidative stress alters lipids, DNA, and proteins, leading to cellular inflammation and programmed cell death, which play an irreplaceable role in physiopathological conditions [98]. *Sargassum ilicifolium* crude lipid extracts demonstrated antioxidant activity in an in vitro experiment [99]. Macroalgae are also considered to be an important source of secondary metabolites and macromolecules with antioxidant activity [100]. Cancer has become a global public health problem over the last few decades [101], and MTCM has made many inspiring achievements and formed a therapeutic system in the field of cancer treatment [102]. The extracts of *Syngnathus* have been found to inhibit tumor cell proliferation, reduce the tumor formation rate, and prolong the survival time of mice [103, 104]. Fucoidan from *Saccharina japonica* and *Undaria pinnatifida* have a significant effect on antitumor activity as well [105]. Undeniably, due to the multitargeted nature of MTCM (especially compound preparations), it has been proven to be effective in treating a wide range of viral diseases [106]. Numerous components in *Sargassum*, including ACE inhibitory peptides and soluble dietary fibers (e.g., fucoidan, porphyran, etc.), could minimize the ACE dominance caused by SARS-CoV-2 infection, enhancing the effectiveness of the COVID-19 vaccine [107]. TCM compound preparations, which contain MTCM, have been verified. For example, *Margaretifera Concha* has now been demonstrated to be effective against influenza and herpes viruses [108]. Pharmacological effects, such as inflammation [109], an anticoagulant effect [110], an antiallergic [111], an antibacterial [112], and even the treatment of obsessive-compulsive disorder [113], etc., have all been verified.

5. Conclusion and Expectation

As a type of TCM with a unique growth environment, an increasing number of experts are conducting studies on MTCM, and the number of publications is growing annually. China, as a pioneer in this field, has carried out a multifaceted, long-term study based on traditional theories (e.g., the processing theory of TCM and the theory of medicinal nature). Research points in other countries are less extensive but more in-depth (e.g., action mechanisms, extraction, and purification of active substances) than research points in China. Meanwhile, the modernization of Chinese research has been aided by scientific thoughts from other countries. By separating the analysis of MTCM according to different medicinal parts, we also found differences in research hotspots between them. Interdisciplinary research can help maximize the benefits of MTCM in the battle against diseases such as cancer, oxidative stress, inflammation, and viral infection. According to recent research hotspots and trends, the return of ancient TCM books, the updating of analytical techniques and tools, the organic integration of the "holistic concept" of traditional medicine and the "individual concept" of modern medicine, the exploration and modification of active ingredients, and the in-depth study of marine organisms (e.g., algae) are all top priorities for all scholars.

The vast majority of MTCM uses plants and animals grown in the ocean as a source of medicine. MTCM as a medicine source is the main difficulty and obstacle to the development of marine medicine, but it can also be the greatest advantage and the strongest foundation for marine medicine [114]. At this stage, accelerating the development and industrialization of marine Chinese medicine is a major problem. From the emergence of Chinese first marine drug (Poly Saccharide Sulphate, PSS®), which was extracted from natural *Sargassum* in 1985 [115], to the proposal of the “Blue Drug Store” development plan in 2016, all these inspiring results showed that MTCM, which originated in China, is merged with modern concepts and embodies a wealth of values. It is undoubtable that “blue pharmaceutical” will become a leading high-tech industry as a result of further in-depth research and development in the field of marine medicine.
Data Availability

Data sharing is not applicable to this research. All data resources were derived from domain resources: https://www.cnki.net/; https://www.wanfangdata.com.cn/index.html; https://lib.cqvip.com/ and https://www.webofscience.com/wos/woscc/advanced-search.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Wenxuan Cao and Jia Liu contributed equally to this work. Peng Yu conceptualized the study; Yulin Dai and Wenxuan Cao handled methodology; Wenxuan Cao was in charge of data collection; Wenxuan Cao handled software; Wenxuan Cao was in charge of visualization; Peng Yu was in charge of funding acquisition; Wenxuan Cao and Jia Liu were in charge of writing the original draft; and Yulin Dai, Jia Liu, Wenxuan Cao and Jia Liu contributed equally to this work. Peng Yu was in charge of writing review and editing.

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Evidence-Based Complementary and Alternative Medicine

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Evidence-Based Complementary and Alternative Medicine


