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Trends in *Euphorbia hirta* Research: A 30-year Bibliometric Appraisal of the Present Realities

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ABSTRACT

Euphorbia hirta L., is a common herb with global spread. Different parts of *E. hirta* are used in traditional medicine for the treatment of a variety of human and animal conditions, such as skin diseases, inflammation, digestive and respiratory disorders. This bibliometric study aimed to provide a panoramic view of the publication landscape in the last thirty years of *Euphorbia hirta* research. VOSviewer was used to analyze 603 documents retrieved from Scopus database during the period, 1992 to 2021. Dominant research themes in the last thirty years were centred on the application of crude extracts or isolated compounds from *E. hirta* against diabetes, oxidative stress, inflammation, tuberculosis, snake bite, gastro-intestinal disorders, respiratory infections, skin pathologies, bacterial, fungal and viral infections. Current paradigm shift in *E. hirta* research are targeted at improving the efficacy of phytomolecules against resistant bacterial pathogens and cancer cells via green synthesis of nanoparticles and the application of *in silico* technologies in predicting the activities of nano-phytomolecules against SARS-CoV-2 and the Dengue virus. This study recommends further research in the determination of the bioavailability of molecules in *in vivo* models. Researchers should carry out more preclinical investigations with the aim of establishing the pharmacokinetic and pharmacodynamic properties of phytocompounds instead of relying solely on *in silico* predictions.

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INTRODUCTION

Since antiquity medicinal plants have been used as a source of medicaments in all cultures. Herbal remedies have become more popular in the treatment of minor ailments, considering the increasing costs of personal health maintenance (Shahid et al., 2013). The successes behind herbal medicines strongly suggests the interaction between bioactive phytocompounds with important biochemical pathways in the human body. Consequently, botanical medicines have become an important research area in drug discovery (Basu et al., 2017). According to the World Health Organization (WHO), more than 80% of the world's population, especially those living in developing countries rely on phytomedicines for their health care needs (Oyebode et al., 2016)

Euphorbia hirta L. (Euphorbiaceae) is a herbal plant with rich structural variability and worldwide distribution. It is a prostrate herbaceous annual weed (Ernst et al., 2015). *Euphorbia hirta* is considered beneficial for its diverse applications in traditional medical systems. According to many ethnomedicinal literatures, decoctions of *Euphorbia hirta* have been traditionally used for the treatment of different ailments such as menstrual disorders, cough, coryza, bronchitis, asthma, helminthiasis, dysentery, jaundice, acne, gonorrhea, peptic ulcers, diabetes, and tumors (Kumar et al., 2010; Promprom and Chatan, 2018).

Additionally, it has been reported that the aerial parts of *E. hirta* were used to treat carbuncle, a skin disease caused by methicillin resistant *Staphylococcus aureus* (Mahato et al., 2019), aqueous-methanol extracts of *E. hirta* have shown antihypertensive activity (Ali et al., 2021). Other pharmacological activities of E. hirta extracts include anti-inflammatory and anxiolytic properties (Xia et al., 2018), antioxidant and antidiabetic activities (Aquino et al., 2020), estrogenic effect (Promprom and Chatan, 2018), immune boosting properties (Pratheepa and Sukumaran, 2014), anticancer activities (Elankanni et al., 2021; Rajabi et al., 2021), anti-filariasis activity (Ndjonka et al., 2013), skin care (Gani et al., 2020), antimalarial activity (Shah et al., 2019), antiviral activities (Saleh and Kamisah, 2021), anti-gout

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activity (Abu Bakar et al., 2020), contraceptive and spermicidal properties (Oguejiofor et al., 2021), sedative activity, diuretic properties, anti-allergic, anti-venom, wound healing activities (Kausar et al., 2016), and antibacterial properties (Akram et al., 2020; Bennet et al., 2020).

The phytochemical compositions of *E. hirta* along with its pharmacological properties have been investigated by many researchers. Specialised metabolites such as saponins, sterols, terpenes, alkaloids, tannins, terpenoids, phytosterol, alkanes, steroids and flavonoids have been found in the aerial parts. The plant is also rich in minerals such as zinc, potassium, calcium and magnesium (Abu Bakar et al., 2020; Fofie et al., 2015; Kumar et al., 2010)

Phytocompounds such as quercetin, quercitrin, quercitol, α-amyrin, ß-amyrin, friedelin, teraxerol, 24-methylene-cycloartenol, ingenol triacetate ß-sitosterol, campestrol, stigmasterol have been isolated from the plant (Tran et al., 2020). Antimicrobial peptides obtained from the leaves of E. hirta have shown antiviral activity against Coxsackievirus A13, Coxsackievirus A20, and Enterovirus C99 (Ogbole et al., 2021)

There are however safety concerns with regards to the use of E. hirta decoctions. Gotep et al. (2018) reported E. hirta toxicity in Baby Hamster kidney (BHK) cells, and deleterious effects in the liver and kidneys of albino rats. Hence, safe doses of E. hirta must be established before consumption.

Bibliometrics is the quantitative method of citation and content analysis for scholarly journals, books and researchers (Cooper, 2015). The quantitative impact of a given publication is appraised by measuring the amount of times a certain work is cited by other resources. Indeed, scholarly periodicals can be mined for authorship, institutional affiliation, and intellectual influence (Pendlebury, 2010; Yang et al., 2021). Bibliometrics and visualization software are effective tools for analyzing a collection of literatures. VOSviewer is a software tool for constructing and visualizing bibliometric networks, which can be used to construct maps of authors, journals, institutions, countries and keywords (Hérubel, 1999; Van Eck et al., 2007). Bibliometric techniques have been previously used to analyse medicinal plant research trends and reveal gaps suggestive of new research focus for researchers (Elisha et al., 2021; Viljoen et al., 2019). Example of some medicinal plants subjected to bibliometric assessment include *Aspalathus linearis* also known as rooibos tea (Elisha and Viljoen, 2021), *Jatropha curcas* (Pereira et al., 2018), *Polygonati rhizoma* (Jiang et al., 2016), and *Curcuma longa* (Ahmed et al., 2018). Within the perimeter of our literature search there are no reports of bibliometric evaluation on *Euphorbia hirta* publications within the timeline set in this study. Hence this study analyzes and explores the performance of authors, institutions, countries, sources of publication, research hotspots and other frontiers during the 30-year period of *E. hirta* research.

MATERIALS AND METHODS

Data source

Data was retrieved from Scopus database (https://www.scopus.com) on the 22nd January 2022. Keywords such as "*Euphorbia hirta*" was searched in the – Title-Abstract-Keyword field. The edited dataset was saved as *.csv file and exported to visualization of similarities viewer (VOSviewer) for further bibliometric analysis. VOSviewer is a free licensed user-friendly software. It is Java powered and able to generate high-resolution visual images of bibliographic networks. The software offer opportunities for researchers to examine bibliographic work (van Eck and Waltman, 2010).

Data analysis

Methods used by Elisha and Viljoen (2021) were adopted with some modifications. Documents retrieved were analysed using the Scopus built-in function to "analyse data", while VOSviewer was used to evaluate the co-occurrence of terms in the title and abstract field, generate term maps and explore bibliographic data for research themes. The data was divided into three decades in order to determine the developmental trends in *Euphorbia hirta* research from 1992 to 2021. Default settings and in some instances, parameters were adjusted in order to construct and analyse network maps and other visualisations.

RESULTS AND DISCUSSION

Summary of the data retrieved from Scopus database on *Euphorbia hirta* research (1992-2021)

Analyses of the 603 publications retrieved from Scopus database on E*uphorbia hirta* indicated that 86.4% of the documents were full research articles, 10% were review papers, 3.6% consisted of conference papers, book chapter, short survey, journal editorial, notes and conference reviews. The publications had 12218 citations. The documents cover a wide range of subject areas, which includes pharmacology, toxicology and pharmaceutics (42.0%), agriculture and biological sciences (32.5%), medicine (27.5%), biochemistry, genetics and molecular biology (20.7%), chemistry (8.5%), immunology and microbiology (8.3%), veterinary sciences 3.0%) and other areas that do not directly fit into this study. Three hundred and twenty-nine (329) sources contributed in the publications of *E. hirta* research findings in the last 30 years. The journals were divided into 154 different clusters based on their link and similarity in the scope covered.

Global publication growth in *Euphorbia hirta* research, 1992-2021

Publication output in the three decades of *E. hirta* research could be described as modest. The total publications recorded in the

first decade (1992-2001) was 33 with 1659 citations. The second decade (2002-2011) recorded 175 papers, with 5434 citations, and the third decade (2012-2021) recorded 395 documents with 5125 citations. The average annual publication in the 30 years of *E. hirta* publications is 20 articles per year. Consequently, the global publication growth rate was 18.6 percent. We observed a slow rise in publications in the first two decades, and a resurgence in published material in the third decade. Precisely, the period 2009-2021, recorded an appreciable increase in annual publications, with an average of 38 publications per year during the period under consideration. The years 2020 and 2021 recorded the highest number of publications in a decreasing order of 54 and 52 publications respectively (**Fig. 1**).

The general surge of publications during the 2020-2021 period could be attributed to the global lockdown and travel restrictions observed due to the COVID-19 pandemic. During the pandemic there were spurious speculations that many scientists were at that time either translating their recorded research findings into articles or were writing reviews; we presumed that many scientists had ample time for such ventures. To corroborate this statement, Else, (2020) reported that there was speedy review of articles, especially those related to COVID-19, and a sharp increase in articles on all subjects submitted to journals during the period. Another reason could be the overwhelming use of *in silico* technologies especially molecular docking to predict the mechanism of action of phytomolecules against SARS-CoV-2 and the rapid selection and development of herbal extracts for the cure and prevention of COVID-19 infections.

Analysis of the performance of countries

Eighty (80) countries contributed in *E. hirta* publications from the information retrieved from Scopus database. India was the most productive country with 273 publications and 4892 citations; distantly followed by Malaysia with 47 publications and 1181 citations, next is Nigeria (42 publications:783 citations) and Pakistan (40 articles with: 753 citations) respectively. (**Fig. 2**), shows the map of the world with the different publication weights of the participating countries.

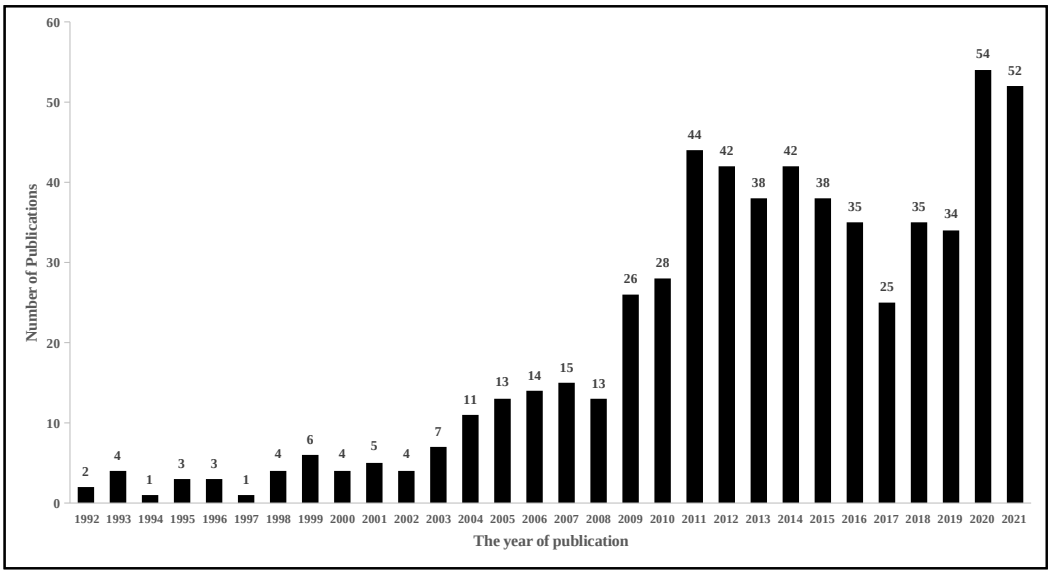

Fig. 1: A 30-year annual growth rate of *Euphorbia hirta* publications retrieved from Scopus database (n = 603)

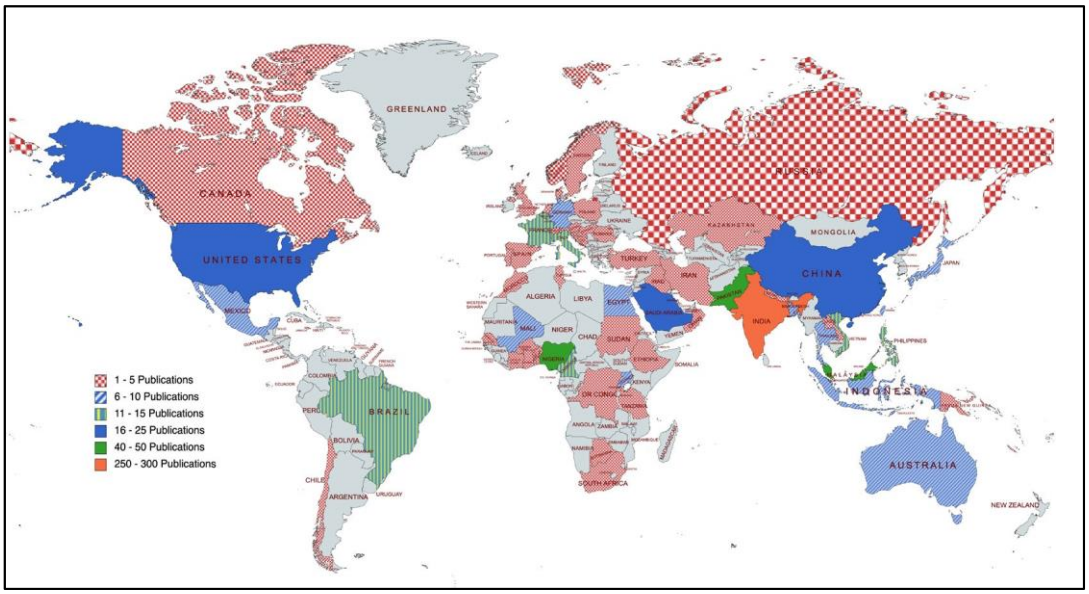

Fig. 2: Map of the world showing the publication weight of the countries involved in *Euphorbia hirta* research in the past 30 years, documents retrieved from Scopus database

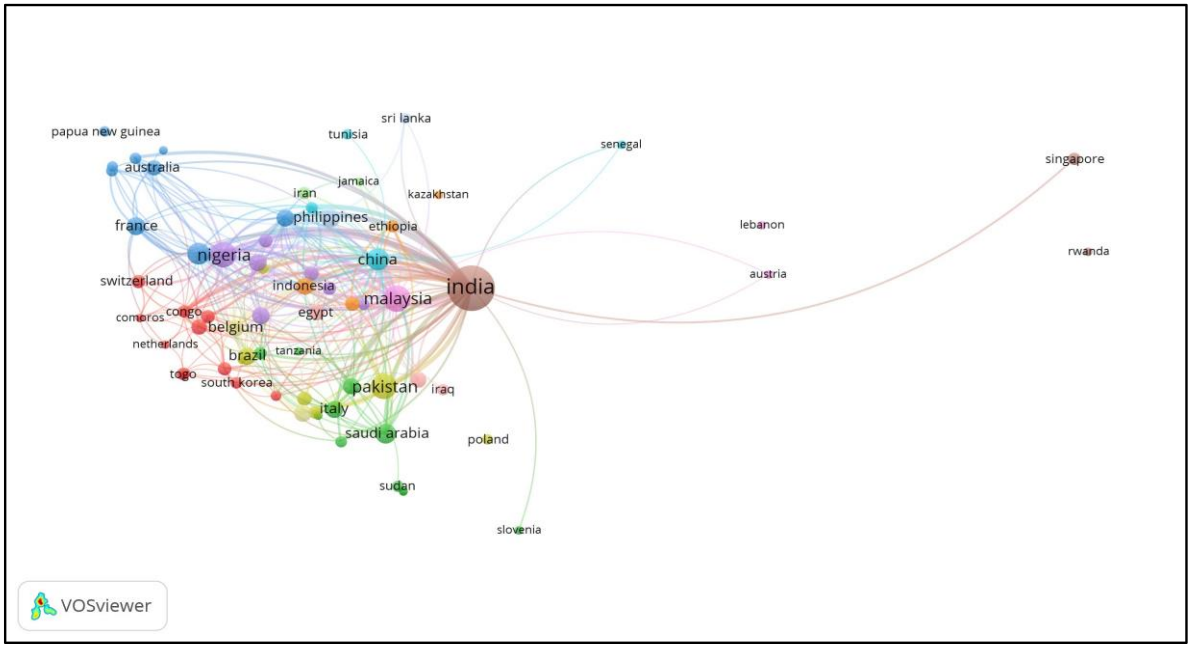

Fig. 3: Network visualization of the countries active in *Euphorbia hirta* research in the past 30 years from publications retrieved from Scopus database 1992-2021

Network visualisation from VOSviewer does not only display the publication output, represented by nodes or bubbles, but it also reveals the interconnectivity of the different items, indicated by the closeness of the bubbles and the thickness of the curved lines. The closer the nodes the stronger their connection with regards to research focus and the thicker the curved lines the stronger their association or in a more technical term, the stronger the collaborative efforts of the two countries or organisations (van Eck and Waltman, 2018).[39] The network visualisation reveals that India has a very strong research collaboration with Malaysia, shown by the thickness of the curved line and closeness of the nodes **(Fig. 3).** This is followed by the United States, Saudi Arabia, Nigeria, Japan, Portugal, China, Philippines, Italy, and Viet Nam connecting to India. Also, on the map can be seen countries with poor collaborative efforts, which are divergently located (**Fig. 3**). For example, Singapore has association with India only, Rwanda (India), Slovenia (India and Saudi Arabia, Senegal (China and India), Papua New Guinea (Spain), Lebanon (India and Malaysia) and Austria (India and Malaysia) respectively. Majority of the countries in the map are convergently located, indicative of close connection or strong total link strength. This is a very positive sign in the progression of *E. hirta* research activities.

With the increase in the global need for the discovery of alternative, potent and safe drugs to meet the challenges of drug resistance and emerging pathogens, it is pertinent to encourage multidisciplinary research collaborations. This we suppose has the proclivity to improve the quality of medicinal plant research output. Jappe et al. (2018) reported that experts from different fields of endeavour can influence the translation of medicinal plant research findings into potent medicaments for the treatment of both human and animal diseases. Consequently, we drilled down into the different nuclei of the 273 publications by Indian authors, and found that India collaborated with 32.5% of the countries that participated in *E. hirta* research in the past three decades. This is indeed an impressive fit and an indication of the continuous efforts to improve phytotherapeutic research. It is a well-established fact that botanical medicines are the oldest known remedies to the human kind, and India is the global hub for ayurvedic treatments. It is the opinion of the authors that the motivation for the high *Euphorbia hirta* research in India might be predicated on the claims of its use traditionally for the treatment of female disorders, respiratory ailments, worm infestations in children, dysentery, jaundice, pimples, gonorrhoea, digestive problems and tumour. In addition, reports of the presence of specialised metabolites such as alkanes, triterpenes, phytosterols, tannins, polyphenols, and flavanoids in the crude extracts of *E. hirta* might influence this activities.[5]

Contributions and association of institutions in the 30 years of *Euphorbia hirta* publications

Using the VOSviewer, we discovered that 1390 institutions contributed in all published documents. These institutions were divided into 503 clusters based on their connections **(Fig. 4)**. The profile of the top five most productive institutions in the three decades of *E. hirta* research includes the University of Science, Malaysia, which have 16 publications and 560 citations. Publications from the institution were centred on phytochemistry, cell culture assays, and antimicrobial investigations. A large volume of the publications were in association with local collaborators, international collaborators are from Australia, India and Japan. Ranked second among the most productive institutions is Quaid-i-Azam University in Pakistan, which had 14 publications and 520 citations. The area of expertise based on published documents includes phytochemistry, antidiabetic and antimicrobial research, and delivery of herbal preparations using nanoparticles. They have a strong institutional collaboration with China, Oman, Mexico, Nigeria, Saudi Arabia and the United States of America. Third on the ranking is the King Saud University in Riyadh, Saudi Arabia, with 12 publications, and 158 citations. The University has expertise in cell culture investigations, antiviral activity,

immunomodulatory investigations and the application of herbal remedies to general gastrointestinal complaints. The King Saud University has a strong collaborative association with institutions in Egypt, India, Pakistan, Oman, China, Nigeria, Sudan, Tunisia and the United Kingdom. The University of Ibadan in Nigeria is ranked 4th with 10 publications and 171 citations. Publications from the University are centred on antiviral, anticancer, antimalarial, and anti-trypanosomal activities. The university has a strong representation in veterinary sciences and animal reproduction studies. We observed its strong link to institutions in Switzerland and the United States of America. The University Putra Malaysia is ranked 5th with 10 articles and 248 citations. Publication affiliations include institutions from Bangladesh, Egypt, Iran and Iraq. Publications are centred on bioherbicidal investigations, fisheries, veterinary sciences and animal feed research.

Authors productivity in the last 30 years of *Euphorbia hirta* research

Euphorbia hirta research and publications in the past 30 years involved 2173 researchers/authors from eighty (80) different countries, divided into 770 cluster based on associations. A closer view at the performances of the authors revealed that only 21 authors (approximately 1.0%) published ≥ 5 documents in the past 30 years. The most productive author has nine publications at the time of writing. Further drill down on the authors contributions indicated that 48 (2.2%) of the authors have ≥ 4 publications, 108 (approximately 5.0%) of the authors have ≥ 3 publications, and 317 (14.6%) have ≥ 2 publications respectively.

The top five most productive authors, their affiliations, area of expertise from published works and countries of co-authorship association are presented as follows. Ranked first is Sasidhran Sreenivasan with 9 publications, and 483 citations. The author is currently affiliated with the University of Science Malaysia, in Malaysia. The author's expertise includes phytochemistry and toxicology; his international co-authorship connection is with authors from Australia, India and Japan. The second most productive author is Diallo Drissa with 6 publications and 250 citations. The author is an affiliate of Institut National de Recherche en Santé Publique Mali, in Bamako, Mali. His publications proclivities are ethnopharmacological studies. His international co-authorship association is with authors from Norway, United Kingdom, France, Netherlands, and the United States. Thirdly placed is Qureshi Rizwana Aleem, with 6 publications and 214 citations. The author is affiliated with the Gujarat University Ahmedabad in India. His publications are centred on phytochemistry and antimicrobial investigations. The author has co-authorship with scientist in Pakistan only on the subject of *Euphorbia hirta*. The fourth position is occupied by two authors – Mahmud Roziahamin and Perumal Shanmugapriya, both with 6 publications and 74 citations. They share the same affiliation – the University of Science Malaysia, in Malaysia. They also share the same expertise, with mechanistic antibacterial studies. The two authors share the same cluster. Their co-authorship association is with authors from local institutions in Malaysia. The author that ranked fifth is Bach Le Thi, affiliated with the University College of Natural Sciences Can Tho, in Viet Nam. The author has 6 publications with 45 citations. The authors publications are centred on the use of herbal extracts to improve fish health and productivity. His international co-authorship is with authors from Belgium.

Despite having few publications some of the authors have appreciable citations. For brevity, we mentioned only authors with more than 300 citations. They include Apers Sandra (Belgium), De Bruyne Tess E (Belgium), Mesia Kahunu (DR Congo), Pieters Luc AC (Belgium), Tona Lutete (DR Congo) and Vlietinck Arnold AJ (Belgium) each with 481 citations, Totte Jozef (Belgium) with 357 citations, Ignacimuthu Savarimuthu (India) with 307 citations. Among these are also, Zarzuelo Antonio (Spain) and Crespo M Esperanza (Spain) each with 304 citations (**Fig. 5**).

The top 20 most relevant papers in *Euphorbia hirta* publications

The twenty (20) most relevant papers in the 30 years of *E. hirta* research were selected using VOSviewer. The software is an important tool that assist academicians select documents

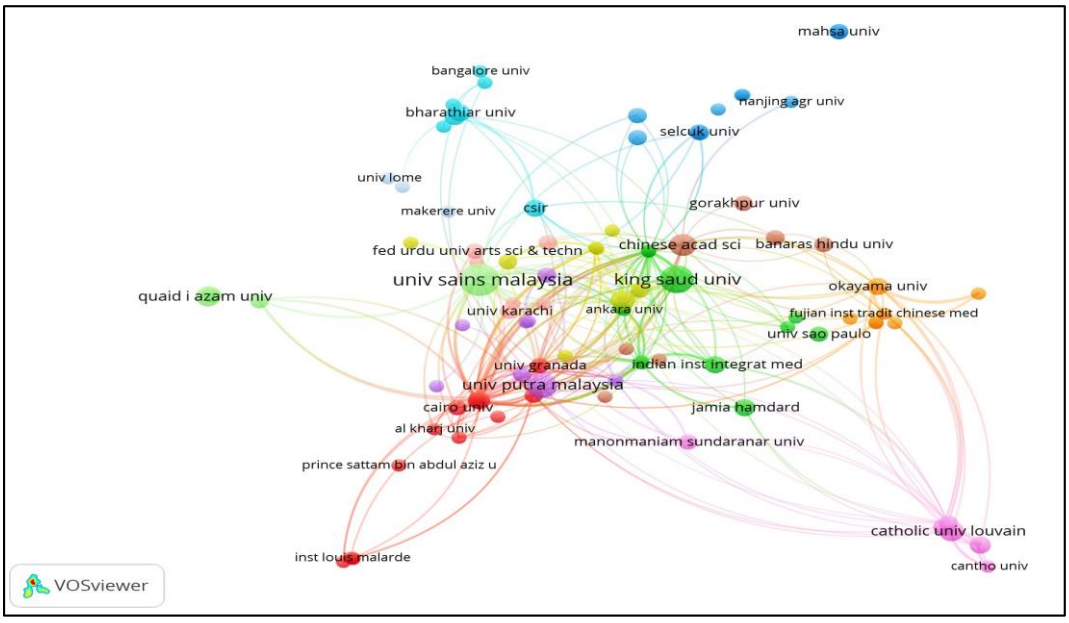

Fig. 4: Network visualisation of the most productive institutions and organizations in the 30 years of *Euphorbia hirta* research

that accurately fit a field of study. The algorithm compares the total link strength (TLS), connection or relationship of the chosen items to one another, the match of the article to the search term in the bibliographic search and citation score of the document. These factors help in choosing appropriate papers. In **Table 1**, the ranking of the papers is not linked exclusively to the citation score, but it is predicated on the strength of association with other documents in the pool. Most recent papers could be ranked higher than a paper with high citation, because of its connection with documents in the research field either as references used or similarity in the title, in some cases the composition of the co-authors in a document, the higher the similarities of the considered factors the higher the ranking. An illustration to further explain this condition is the article titled 'Antimicrobial activity of certain Indian medicinal plants used in folkloric medicine' author by Srinivasan et al. 2001, published in Journal of Ethnopharmacology 74(3):217-220. This paper is ranked first from Scopus list because of its citation score of 457 as the most cited papers in *Euphorbia hirta* research. However, upon closer inspection we discovered that the title of the paper has no mention of the plant in question, the article keyword does not bear it, there is no mention of *Euphorbia hirta* in the article abstract. There is only a modest mention of *Euphorbia hirta* in the body of the text in the table 1 of the article. In this particular case the plant was erroneously classified as not having antimicrobial activity against the tested pathogens. This conclusion is actually attributed to the method used; microdilution method would have given a different result as we observed in other reports. The use of agar gel diffusion does not adequately give the accurate result of the antibacterial activity of a plant extract, as some extracts do not diffuse through the agar gel or may poorly diffuse through the gel to elicit any significant antibacterial effect (Eloff, 1998). In this case the aqueous extract of the whole plant. VOSviewer is able to sort some of these discrepancies and select the most relevant documents (van Eck and Waltman, 2018; Van Eck and Waltman, 2014). Further, analysis of the selected articles indicated that full research articles formed 90% of the top 20 papers and 10% reviews. These statistics are almost reminiscent of the categorisation of the 603 documents earlier mentioned. This is suggestive of research progress and the willingness to share original research work with other researchers. Worthy of note is that the top 20 papers cumulatively make up 12.7% of the total citations. This is an attestation to their quality and impact. Sixteen (16) journals contributed in the publications of the top 20 papers (**Table 1**). The Journal of Ethnopharmacology contributed 20% of the top papers followed by Fitoterapia (10%). The authors of the top 20 documents came from 13 countries. Authors with affiliations in India contributed in 40% of the articles, while authors from Belgium and Democratic Republic of Congo contributed 15% each. The top 20 articles coloured the research landscape with publications centred on antimalarial, antibacterial, antifungal, antidiabetic, antiplasmodial, wound healing, analgesic, anti-inflammatory, anti-amoebic, antiretroviral (anti-HIV), antioxidant and antidiarrhoeic activities.

Overview of terms and keywords from documents retrieved from Scopus database

The binary counting function was used in the term analysis. Binary counting means that only the presence or absence of a term in a document matters. The total number of a term in a document is not taken into account (Van Eck and Waltman, 2014). Maps were created from terms in the title and abstract fields. The minimum number of occurrences in the three decades were adjusted so as to have sufficient items for analyses. For the 1st decade, the minimum occurrence for an item was from 1, while for the second decade the minimum occurrences was adjusted to ≥ 3, for the third decade it was adjusted to ≥ 5. The terms identified in the first decade was 987, after the 60% most relevant term calculation and manual screening of terms that fit our analysis, only a dismal 17 terms were used to create the map and clusters. For the second decade, 4752 terms were identified and only 76 terms were chosen to create the network and clusters. In the third decade, 11309 terms were identified, from which 135 terms were selected for further analysis after exclusions. The number of

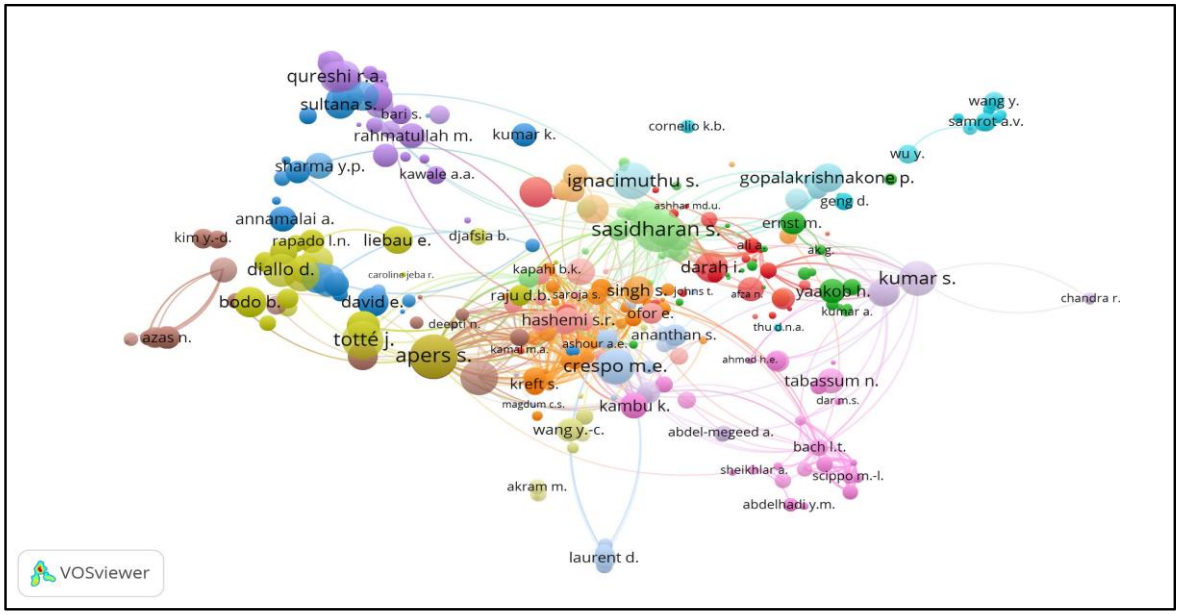

Fig. 5: Network visualization of influential authors in the 30 years of *Euphorbia hirta* research from documents retrieved from Scopus database. (Authors are categorized into 18 different clusters)

Table 1: The 20 most relevant publications in the last 30 years of *Euphorbia hirta* research as determined by VOSviewer

Ranking	*Author and Year*	*Document Details*	*TC*	*DT*	*Link*	*Country*
1	Kumar et al. 2010	*Euphorbia hirta*: Its chemistry, traditional and medicinal uses, and pharmacological activities. Pharmacognosy Reviews, 4(7):58-61	119	R	53	India
2	Liu et al. 2007	Antimalarial flavonol glycosides from *Euphorbia hirta*. Pharmaceutical Biology 45(4):278-281	53	A	39	China, Japan, Portugal
3	Johnson et al. 1999	*Euphorbia hirta* leaf extracts increase urine output and electrolyte in rats. Journal of Ethnopharmacology 65(1):63-69	59	A	34	Nigeria
4	Galvez et al. 1993	Antidiarrhoeic Activity of *Euphorbia hirta* extract and isolation of an active flavonoid constituent. Planta Medica 59(4):333-336	221	A	29	Spain
5	Hore et al. 2006	Effect of aqueous *Euphorbia hirta* leaf extract on gastrointestinal motility. Fitoterapia 77(1):35-38	36	A	27	India
6	Kausar et al. 2016	Review of the phytochemical and pharmacological activities of *Euphorbia hirta* Linn. Pharmacognosy Journal 8(4):310-313	12	R	22	India
7	Ogbulle et al. 2007	Antibacterial activities and toxicological potentials of crude ethanolic extracts of *Euphorbia hirta*. African Journal of Biotechnology 6(13):1544-1548	46	A	22	Nigeria
8	Basma et al. 2011	Antioxidant activity and phytochemical screening of the methanol extract of *Euphorbia hirta* L. Asian Pacific Journal of Tropical Medicine 4(5):386-390	118	A	20	Malaysia
9	Rajeh et al. 2010	Assessment of *Euphorbia hirta* L. leaf, flowers, stem and root extracts for their antibacterial and antifungal activity and brine shrimp lethality. Molecules 15(9):6008-6018	59	A	20	Malaysia, India
10	Vijaya et al. 1995	Antibacterial effect of theaflavin, polyphenon 60 (*Camellia sinensis*) and *Euphorbia hirta* on *Shigella spp*.- a cell culture study. Journal of Ethnopharmacology 49(2):115-118	86	A	19	India
11	Sudhakar et al. 2006	Antimicrobial activity of *Caesalpina pulcherrima*, *Euphorbia hirta*, and *Asystasia gangeticum*. Fitoterapia 77(5):378-380	80	A	17	India, Ethiopia
12	Singh et al. 2006	Inhibition of early and late phase allergic reactions by *Euphorbia hirta* L. Phytotherapy Research 20(4):316-321	25	A	17	India
13	Tayone et al. 2014	Isolation and structure elucidation of potential anti-dengue metabolites from tawa-tawa (*Euphorbia hirta* Linn.). Walailak Journal of Science and Technology 11(10):825-832	6	A	16	Philippines, Japan
14	Subramanian et al. 2011	Antidiabetic and antioxidant potentials of *Euphorbia hirta* leaves extract studied in streptozotocin-induced experimental diabetes in rats. General Physiology and Biophysics 30(3):278-285	21	A	16	India
15	Tona et al. 1999	Antimalarial activity of 20 crude extracts from nine African medicinal plants used in Kinshasa, Congo. Journal of Ethnopharmacology 68(1-3):193-203	161	A	16	DR Congo, Belgium
16	Shih et al. 2010	A molecular pharmacology study into the anti-inflammatory actions of *Euphorbia hirta* L. on the LPS-induced RAW 264.7 cells through selective INOS protein inhibition. Journal of Natural Medicine 64(3):330-335	39	A	15	Taiwan
17	Tona et al. 2000	Antiamoebic and spasmolytic activities of extracts from some antidiarrhoeal traditional preparation used in Kinshasa, Congo. Phytomedicine 7(1):31-38	126	A	15	DR Congo, Belgium
18	Wu et al. 2012	Phenols and flavonoids from the aerial part of *Euphorbia hirta*. Chinese Journal of Natural Medicines 10(1):40-42	50	A	14	China
19	Tona et al. 2004	*In vitro* antiplasmodial activity of extracts and fractions from seven medicinal plants used in Democratic Republic of Congo. Journal of Ethnopharmacology 93(1):27-32	196	A	14	DR Congo, Belgium
20	Gyuris et al. 2009	Antiviral activities of *Euphorbia hirta* L. against HIV-1, HIV-2 and SIV_{mac251}. In vivo 23(3):429-432	42	A	13	Hungary

TC = Total citations; DT = Document Type

identified terms in the three different decades suggest growth in the research coverage, with an increase of 17.3% during the period under review.

Term map in the first decade (1992-2001)

There were only two clusters in the 1st decade. The first cluster is coloured red, and comprises 53.0% of the connected terms. The cluster is best described as bioactive evaluations of molecules. Reported activities include publications on anticholinesterase inhibitory activity, and the determination of antibacterial activities using the paper disc method on mostly Gram negative bacterial pathogens. The second cluster is coloured green and comprised of 47.0% of the connected terms. The cluster can be broadly described as reports on

the elementary extraction of *E. hirta* using different solvent systems (**Fig. 6**).

Term map in the second decade (2002-2011)

In the second decade, 5 clusters were identified and classified based on the connection and association of the terms. The 1st cluster is coloured red and comprised of 26.3 % of the total terms. The clusters reflects antimicrobial activity. During this period the use of broth microdilution method replaced the use of paper disc observed in the first decade. Here the minimum inhibitory concentration of the extracts were determined for their antibacterial and antifungal activities. An improvement in this era is the use of clinical isolates as test pathogens in the antimicrobial assays. Clusters 2, is coloured green and made up of 25.0% of all terms. Publications on the antioxidant determination of *E. hirta* extracts dominated the landscape. The cluster consist of hybrid publications composed of phytochemical analysis of secondary metabolites and lipid peroxidation inhibition activities of extracts. Cluster 3 which is coloured blue in the map is composed of 18.4% of the chosen words. It is composed of high volume of publications best classified under ethnobotanical surveys. Surveys of plants used against rheumatism, diarrhoea, respiratory and skin diseases from different regions of the world were dominant. The fourth cluster is coloured olive and made up of 15.8% of the terms. The cluster represents publications on antimalarial/antiplasmodial activity of *Euphorbia hirta* extracts. Also observed under this cluster were reports on the cytotoxic properties of active compounds and their wound healing properties. The 5th cluster represents publications dealing with the antidiabetic activity of *Euphorbia hirta* extracts. Also represented in the fifth cluster are publications on molluscicidal activity, serum biochemistry and hematology reports. We generally observed an increase in the volume of reported research activities and improvement in research methodologies in this era in comparison to the first decade (**Fig. 7).**

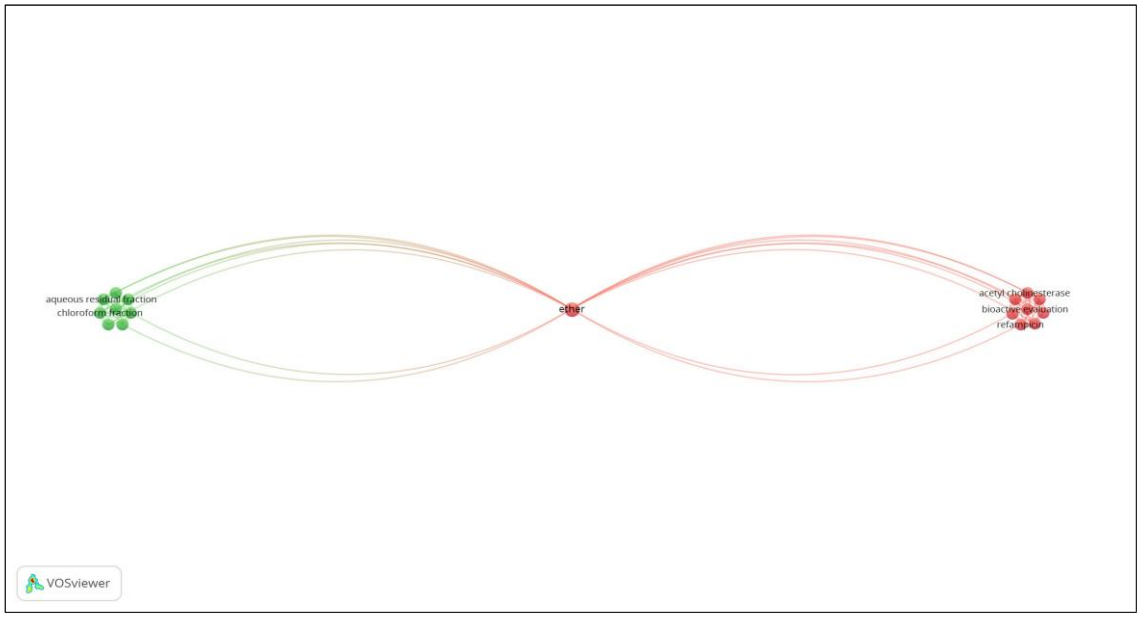

Fig. 6: Term map of the first decade

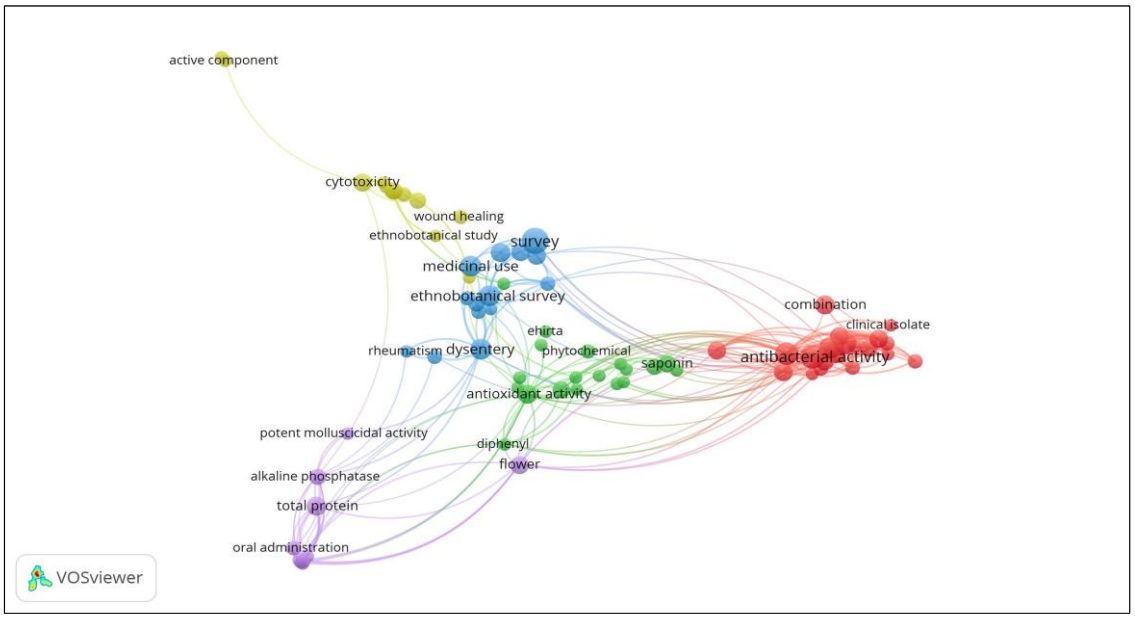

Fig. 7: Term map of the second decade

Term map in the third decade (2012-2021)

In this era we observed improvement and advancement in the *E. hirta* research. The map reflects a large number of terms (**Fig. 8**), indicative of high traffic of research activities. The map is composed of six (6) clusters which represents six different research foci. Cluster 1 is coloured red and it is made up of 28.1% of the terms. The cluster is best defined as ethnobotanical survey. The landscape gives a panoramic view of activities carried out by researchers in the field of medicinal plant research. The reports are predicated on online survey on a plethora of plants including *E. hirta* with antiviral activity and potentials for use as herbal remedies against COVID-19. The second cluster like that of the second decade is best classified under antioxidant activity. Included under this section were antioxidant assays using FRAP, and cytotoxicity assays using the MTT methods. The cluster is made up of 22.2% of the words and it is coloured green. The third cluster is coloured blue and also shared the same weight of terms with the previous cluster (22.2%). This is best described under antibacterial activities. Publications on anticancer activities abound in this cluster. The 4th cluster is coloured olive and made up of 11.1% of the selected terms. The cluster is classified under green synthesis. Here we observed a large volume of publications on the synthesis of silver nanoparticles from extracts of *E. hirta* tested for their antimicrobial and anticancer action. Cluster 5, is also very important in the third decade landscape. It is defined under phytochemical analysis, chromatographic and spectroscopic techniques such as high performance liquid chromatography (HPLC) and nuclear magnetic resonance spectroscopy (NMR). The 6th cluster is coloured turquoise, and comprised of 8.2% of the terms. It largely represents the anti-inflammatory activity publications of *E. hirta* against cytokine storm incriminated in COVID-19 fatalities. There are also publications that highlight anti-hypertensive activity of the plant extracts and heavy metal detection in herbal preparations.

Assessment of publications in the last 5 years and recommendations

Euphorbia hirta research has witness the introduction of quality publications in the last five years. From the term analysis, hybrid papers have included topics like ferric Reducing antioxidant power (FRAP) assays, relative ability of antioxidants from *E. hirta* extracts to scavenge 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) in aqueous phase, *in vitro* effects of phytochemical contents of active extracts on enzymes such as glucosidase, amylase and tyrosinase (**Fig. 9).** Findings also indicated influx of publications related to screenings on specialised metabolites from *E. hirta* against cancer cells. Also included in the plethora of therapeutic reports in *E. hirta* research are efforts in enhancing the potency and efficacy of phytomolecules against bacterial pathogens and cancer cells through green synthesis of silver nanoparticles. Though, there is the need to improve investigation into the safety and toxicity of such remedies. An interesting component of new publications as expected isrelated to molecular docking studies using *Euphorbia hirta* extracts or isolated phytocompounds on SARS-CoV-2, determining the drug likeness properties of such molecules through their inhibition of viral entry and interference with viral replications. There are very few publications on the determination of bioavailability of such molecules in *in vivo* models. More preclinical studies are encouraged to really determine the pharmacokinetics and pharmacodynamics of such molecules, instead of relying on *in silico* predictions. There are also articles that highlight ethnobotanical documents where the therapeutic activities of *E. hirta* are mentioned. Analysis of the overlay timeline map of the most recent inclusions revealed some key areas that either needs more attention or are new concepts that have not been adequately investigated in the past years (**Fig. 9**).

The outbreak of COVID-19 pandemic called for the urgent responses seen through online search for medicinal plants or known polyherbal formulations with antiviral activities

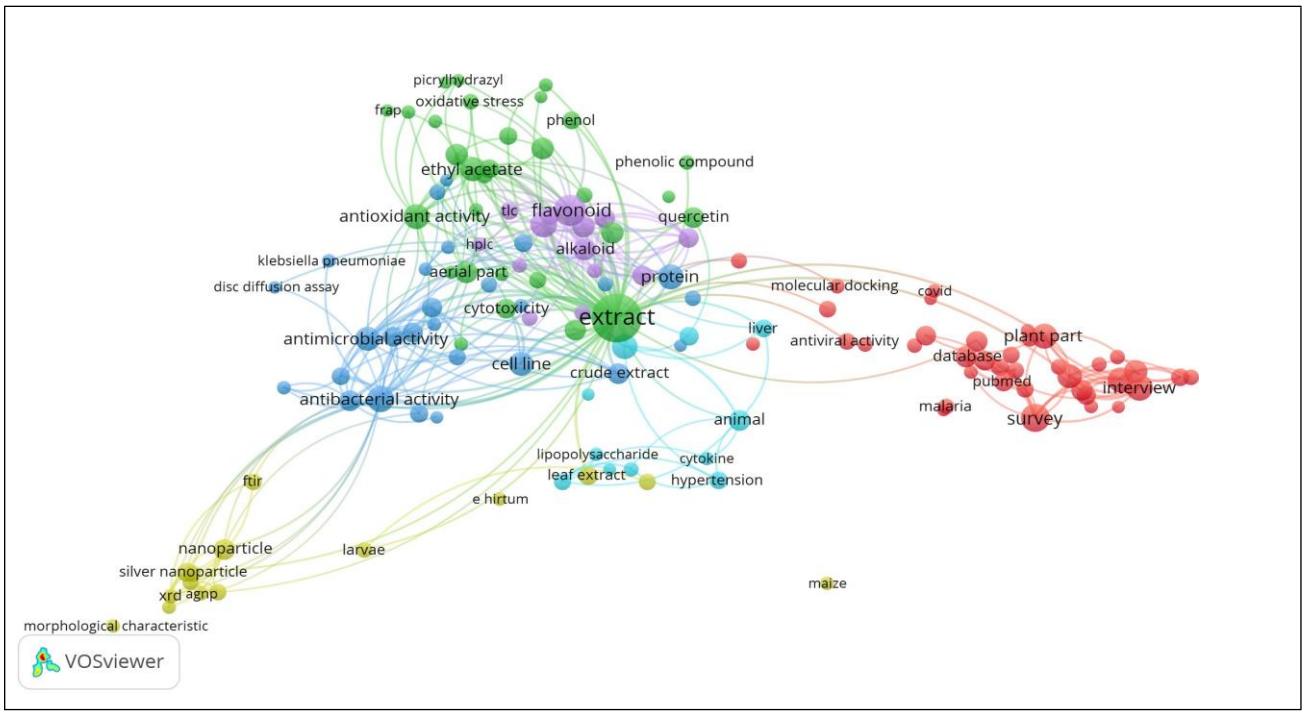

Fig. 8: Term map of the third decade

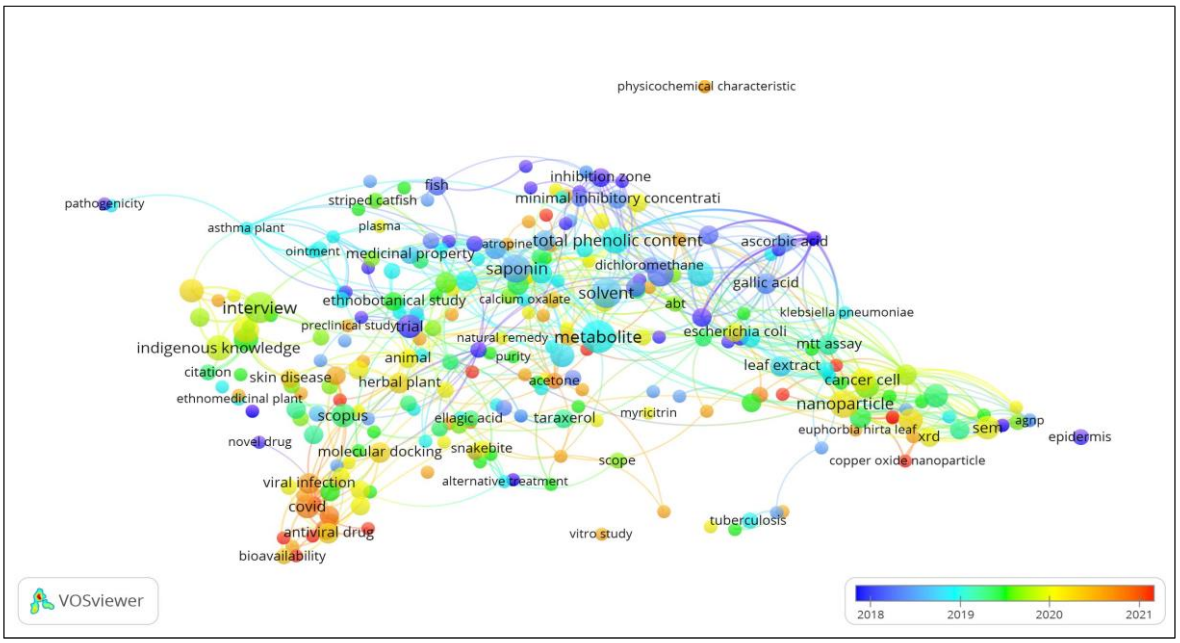

Fig. 9: Overlay timeline of the most recent publications in *Euphorbia hirta* research

or immunity boosting potentials that were seen in published scientific evidences and comprehensive or systematic reviews. There is the need to revisit the screening of herbal extracts against viruses, especially corona and influenza viruses, with the aim to develop potent antiviral drugs or supplements.

Research on *E. hirta* and other medicinal plants needs to be focused on the effects of herbal preparations or isolated bioactive compounds on the pathogenicity and virulence of pathogens, determined through phylogenetic analysis and other molecular techniques such as gene expression. We recommend physicochemical characterisation of fractions or phytocompounds. Antimycobacterial investigation of water extracts has been observed in the new publications. More attention should be channelled to the effects of *E. hirta* on *Mycobacterium tuberculosis*. Another area is in the use of herbal extracts in aquaculture (fish health), their general impact in livestock health and production. Another area of research that needs to be improved upon is the screening of *E. hirta* from active aqueous fractions on anxiolytic activity. Green synthesis of copper oxide nanoparticles and the biological application of nanoparticle in anticancer therapy and against bacterial pathogens such as *Escherichia coli* and *Streptococcus mutans* should be one of the new research focuses.

CONCLUSION

Our bibliometric study indicated modest publication growth rate in the last 30 years of *E. hirta* research. Research gaps observed in this study calls for improved collaborative and multidisciplinary engagement for results with potential translational applications. Extracts of *E. hirta* should be explored for application in the field of veterinary sciences, animal production and aquaculture. Researchers should employ the use of nanotechnology in the effective delivery of phytomolecules in the mitigation of cancers and other infectious agents. We recommend researches directed at the effects of *E. hirta* extracts or isolated compounds on the virulence and pathogenicity of pathogens, especially the SARS-CoV-2 that has affected us globally.

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Authors contributions

Conceptualization and design of the research was carried out by ILE. Data collection and analysis was conducted by ILE and MMS. The first draft manuscript was written by ILE. Critical reading, and review of the final manuscript was carried out by OKF, MMS, SBZ, JGU, HJ, AEI, AEJ, TBK, GJG, ZM, BY and MM. Final approval and contributions for the publication of the manuscript was made by all authors.

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