European Journal of Integrative Medicine 56 (2022) 102197

Contents lists available at ScienceDirect

European Journal of Integrative Medicine

journal homepage: www.sciencedirect.com/journal/european-journal-of-integrative-medicine

Scoping review

Boswellia: Systematically scoping the *in vitro, in vivo* and clinical research

Karen Pilkington [a,*], Geoffrey John Pilkington [b,c,d]

[a] *Independent Researcher and Visiting Senior Research Fellow, School of Health and Care Professions, University of Portsmouth, St Michael's Building, White Swan Road, Portsmouth PO1 2DT, UK*
[b] *Emeritus Professor of Cellular and Molecular Neuro-oncology, University of Portsmouth, St Michael's Building, White Swan Road, Portsmouth PO1 2DT, UK*
[c] *Department of Basic & Clinical Neuroscience, Kings College London, UK*
[d] *School of Pharmacy & Pharmaceutical Sciences, Cardiff University, UK*

ARTICLE INFO

Keywords:
Boswellia
Frankincense
Review
In vitro techniques
Animal experimentation
Clinical trials

ABSTRACT

Introduction: *Boswellia* is a genus of shrubs or small/medium trees in which there is continued interest in a number of species for their potential medicinal use. . This review aimed to produce a 'map' of research on *Boswellia* to identify the potential for translation of research findings across different areas and identify any research gaps.

Methods: Searches were carried out using major databases for *in vitro, in vivo* and clinical studies on any condition or disease, involving *Boswellia* species and extracts. Data were extracted on the health condition or disease, study type, *Boswellia* species and form being investigated.

Results: 5296 records were retrieved resulting in 657 relevant research papers; 297 (45.2%) reported *in vitro* studies, 236 (40.0%) reported *in vivo* studies, and 68 (10.3%) reported clinical studies. Studies were located corresponding to 20 of 21 health research categories, the most frequently researched being Cancer and Neoplasms, Inflammatory and Immune System, and Infection. The species *Boswellia serrata* and *Boswellia sacra* have undergone most investigation. Different forms of *Boswellia* were employed with boswellic acids, specifically Acetyl-11-keto-β-Boswellic acid (AKBA) and 11-Keto-β-Boswellic acid (KBA) generating most interest. Significant numbers of animal studies were located but few clinical studies.

Conclusions: The extent, range and nature of the research on extracts and products derived from *Boswellia* species is revealed. Research is highlighted which may have more widely applicable results (for example on pharmacokinetics, delivery and toxicity), as are current research gaps and potential targets for greater collation of existing data to reduce duplication.

1. Introduction

1.1. *Boswellia species: distribution and naming*

Boswellia is a genus of shrubs or small/medium trees that are distributed across dry areas of tropical Africa, Madagascar, the Arabian Peninsula and Indian subcontinent [1]. Twenty-three species are accepted with some species found primarily in India (e.g. *Boswellia serrata* Roxb.) and others mainly in Africa and Arab countries (e.g. *Boswellia sacra* Flück.). One species restricted to Madagascar and referred to as *Boswellia madagascariensis* Capuron is actually a member of the *Ambilobea* genus [1,2]. Belonging to the family *Burseraceae* Kunth, the genus *Boswellia* Roxb. Ex Colebr. was first described in 1807 and is of major economic importance in countries such as Somalia which harvest the resinous dried sap from species such as *B. sacra* and *Boswellia frereana* Birdw [1]. The International Union for Conservation of Nature has designated a number of *Boswellia* species as vulnerable and there is evidence that *Boswellia* populations are threatened by over-exploitation and ecosystem degradation [3]. For example, *Boswellia papyrifera* (Caill. ex Delile) Hochst., which is a main source of frankincense (the dried resin), has undergone what is described as a 'population collapse' in recent years [4]. Nevertheless, there is considerable continued interest in the potential medical uses of *Boswellia* and a number of species have been investigated in a range of health conditions.

Several species yield frankincense and have been transported over time from one region to another [5]. Consequently, many of the species have been described with different names in different regions which has led to confusion over the taxonomy [6]. Naming of species has evolved

* Corresponding author.
E-mail address: karen.pilkington@port.ac.uk (K. Pilkington).

https://doi.org/10.1016/j.eujim.2022.102197
Received 6 June 2022; Received in revised form 3 October 2022; Accepted 5 October 2022
Available online 8 October 2022
1876-3820/© 2022 The Authors. Published by Elsevier GmbH. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

over time with, for example, one of the species originally described by surgeon and botanist Carter in 1948 [7], hence *Boswellia carteri* Birdw. (also carterii). This is now considered as a synonym for *B. sacra* according to authorities such as Kew Plants of the World Online [1] although, claims had been made that, based on chromatography and spectrometry, the Somalian (*B. carteri*) and Omani/Yemeni (*B. sacra*) species were two distinct species [8].

1.2. Medicinal interest in Boswellia

The aromatic terpenoid oleo-gum resin, known as frankincense or olibanum, may be burnt as incense, or used for chewing or medicinal purposes [1]. In addition to its use as incense in cultural and religious ceremonies, the resin obtained from *Boswellia* has been used traditionally for inflammatory disease, and for its wound healing and antimicrobial properties as well as a wide range of other uses [2]. There is interest in its potential effects on cancer following reports of *in vitro* anticancer activity; in particular, that boswellic acids are cytotoxic to various cancer cells including those involved in glioma [9], leukaemia [10], prostate cancer [11], and colon cancer [12].

Biological activities have been attributed to various constituents of *Boswellia* including the essential oils, with the boswellic acids being a particular focus of attention [13]. Boswellic acids are pentacyclic triterpenoid molecules which are considered to be the most pharmacologically active components of extracts [14]. More than 12 different boswellic acids have been identified with Acetyl-11-keto-β-Boswellic acid (AKBA) and 11-Keto-β-Boswellic acid (KBA) generating most interest [15]. This interest encompasses a potential apoptotic effect on cancer cells and downregulation of cytokines in inflammation [16].

1.3. Previous reviews

Recent reviews have focused on specific species, for example, *B. sacra* (synonym *B. carteri*) [17,18], covering aspects such as chemical composition and pharmacological activity. Khajehdehi and colleagues [19] explored evidence of anti-inflammatory, anticancer, and memory-enhancing effects of frankincense and did not differentiate these effects across different species. Other reviews have addressed the evidence on specific medical conditions including cancer [20] and inflammatory conditions [21], osteoarthritis [22] and Alzheimer's disease [23]. Siddiqui et al's review [23] investigated whether boswellic acids modulate the 5-Lipoxygenase/cyclooxygenase (5-LOX/COX) pathway in arachidonic acid metabolism. Efferth and Oesch's review [21] provides a descriptive overview of a wide range of research and concluded that clinical trials showed the efficacy of frankincense and its phytochemicals against osteoarthritis, multiple sclerosis, asthma, psoriasis and erythematous eczema, plaque-induced gingivitis and pain but that more trials are needed in cancer. Yu et al.'s systematic review [22] focuses solely on randomised controlled trials of osteoarthritis and indicates that '*Boswellia* and its extract may be an effective and safe treatment option'. The seven relatively small trials on which this conclusion was based include several in which *Boswellia* was combined with other agents thus complicating interpretation. *Boswellia serrata* extract has also been assessed for its potential in the treatment of COVID-19 in the elderly [24]. This review explored evidence of effects of *B. serrata* likely to be relevant to COVID-19, for example activity against pulmonary lesions, oxidative stress, inflammation, immune disturbance, viruses, and secondary microbial infection. The majority of reviews drew on evidence from *in vitro, in vivo* and clinical research.

It is clear that there has been significant and increasing interest in *Boswellia* for a range of conditions. It is also likely that results from one area of investigation could be translated across to another, either in terms of the methods used (i.e. whether *in vitro, in vivo* or clinical) or in terms of the findings (e.g. results related to generic effects such as those on inflammation or apoptosis and those on toxicity or pharmacokinetics/delivery of the extract).

This review aimed to produce a 'map' of research on *Boswellia* through searches for and categorising and analysing of relevant research studies to identify where there is potential for translation of research findings across different areas and where there are potential research gaps.

2. Methods

In carrying out a review of research within a specific area, a number of possible approaches are available. Systematic reviews have become the gold standard for answering specific questions by searching, appraising and collating the findings of a set of research studies. The question to be answered by a systematic review needs to be well-defined and this guides the selection of studies which is likely to be limited. Scoping studies, however, can address broader topics where there is likely to be valuable information from a range of study designs and can provide an invaluable first step in identifying future research questions. They are key to understanding the 'volume, nature and characteristics of the primary research' in a specific area [25].

This review was intended as a form of scoping study in addressing a broad area where different designs may have been used. The aim was to reveal the extent, range and nature of the research on *Boswellia* species. Thus, the review was conducted based on the Arksey and O'Malley scoping study framework [25]. It follows the 5 main stages described in this framework:

- Stage 1: identifying the research question
- Stage 2: identifying relevant studies
- Stage 3: study selection
- Stage 4: charting the data
- Stage 5: collating, summarizing and reporting the results

We carried out searches in May 2021 of PubMed, Ovid MEDLINE, Embase, AMED, Cochrane Library, PsycINFO and CINAHL. Searches were from inception of each database. We also searched BIOSIS Reviews to 2008 (only available to this date).

The searches aimed to identify all research including *in vitro, in vivo* and clinical studies on any condition or disease, on *Boswellia* species and extracts. The search strategy for all databases except for BIOSIS Reviews was as follows: *("Boswellia"[Mesh] OR Boswellia OR Boswelia OR boswellic OR boswelic OR frankincense*). For BIOSIS Reviews, the following adapted strategy was used: *Boswellia OR Boswelia OR boswellic OR boswelic OR frankincense (in Topic)*.

Search results were downloaded into Endnote, duplicates (records retrieved from more than one source) were removed and the remaining results screened by abstract and title for all research studies by one researcher (KP). Studies in which the intervention was *Boswellia* combined with another herb, spice or a nutritional product were excluded. Also excluded were: books, case reports, commentaries, conference abstracts, letters, protocols, reviews, studies solely reporting on chemical constituents, surveys except where *Boswellia* was specifically mentioned in the abstract and studies published in languages other than English. Data was extracted on the following for each study: health condition or disease providing a focus for the study; study type (including whether animal or human cells were used in *in vitro* studies); *Boswellia* species and form being investigated. Where papers reported more than one study type, for example an *in vitro* study followed by an *in vivo* study, these were counted as separate studies. Research studies were then categorised by the disease/disorder using UKCRC Health Research Classification System [26]. The 21 categories cover all diseases, conditions and areas of health with each health category including research into disease and normal function. A further category (Diet, Obesity and Nutrition) was used for studies focused on obesity. Each paper could be categorised under one or more categories. For example, a paper that focused on anti-inflammatory effects and pharmacokinetics was included both relevant categories. Similarly, if an *in vitro* study and an *in*

vivo study were both described in a paper, these were counted as separate studies for the purposes of categorisation. Naming of species followed those accepted in the Plants of the World Online reference source [1].

3. Results

The searches retrieved a total of 5296 records of which 2592 were duplicate records retrieved from more than one source. Thus, 2704 unique records were screened for research studies. Six hundred and eighty-nine potentially relevant records were selected and 32 of those were excluded based on the full-text of the article (numbers and reasons shown in Fig. 1). Therefore, 657 papers were included and these had been published between 1969 and 2021.

3.1. Study types

A total of 657 papers reporting research studies of *Boswellia* were identified. Of these, 297 (45.2%) reported *in vitro* studies, 236 (40.0%) reported *in vivo* studies, and 68 (10.3%) reported clinical studies and 4 (0.6%) papers reported *ex vivo* or *in silico* studies. Fifty-one (7.8%) papers reported more than one study type (e.g. both an *in vitro* and an *in vivo* study).

3.2. Health categories

Studies were located corresponding to 20 of the 21 health research categories. The only two categories for which no studies were located were 'Congenital Disorders' and 'Ear'. 'Cancer and Neoplasms' was the most frequently researched health category, followed by 'Inflammatory and Immune System', and then 'Infection'. Other categories in which there were more than 50 studies included 'Neurological', and 'Oral and Gastrointestinal'. The most frequently researched topic using *in vitro* methods was 'Cancer and Neoplasms' while 'Inflammatory and Immune System' was the most frequently researched using *in vivo* methods. Fewer clinical studies were located: of these only two categories included more than 10 studies. These were the 'Neurological' and the 'Musculoskeletal' categories. Within each category, a range of different

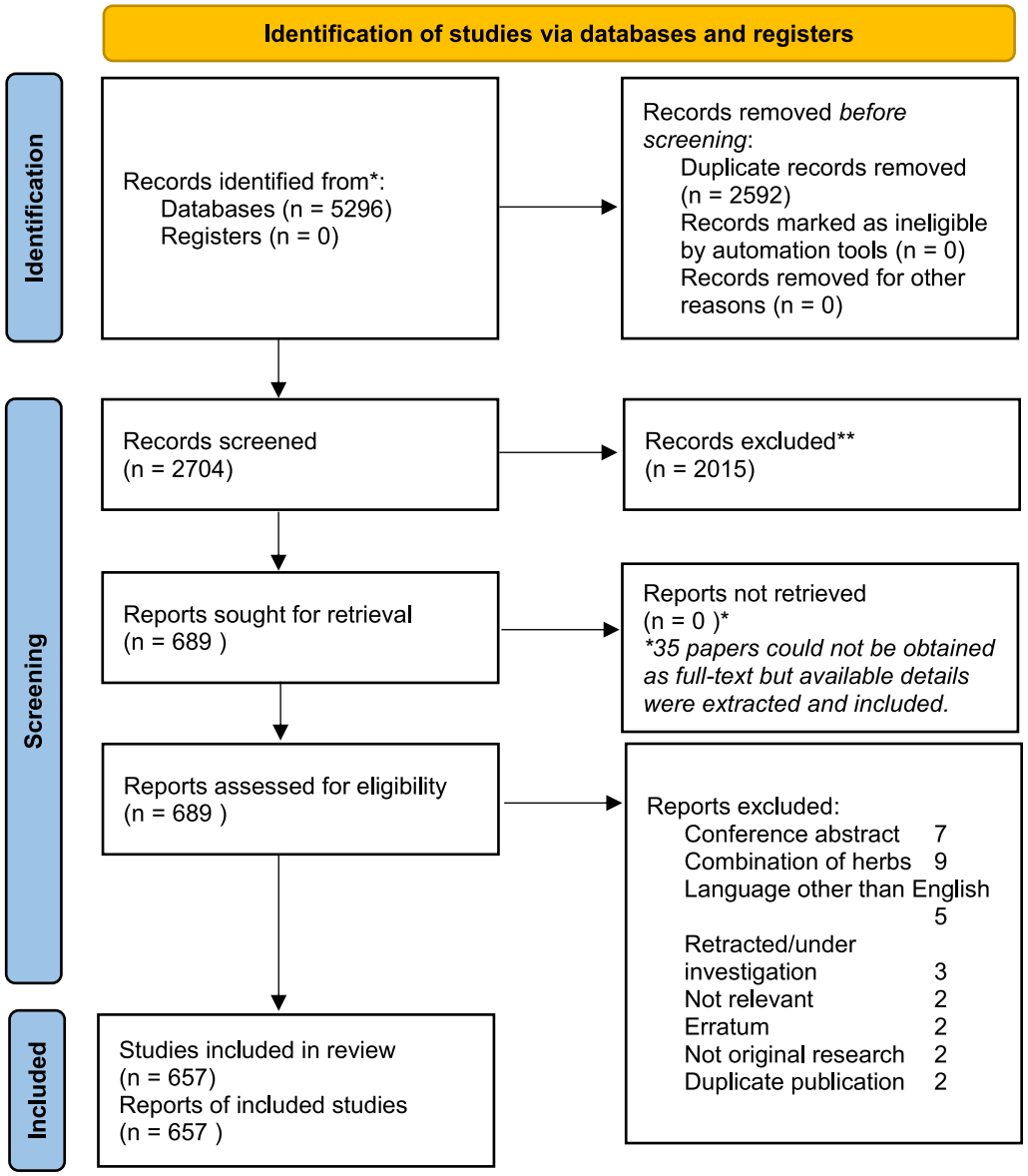

Fig. 1. PRISMA 2020 flow diagram.
From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi:10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

diseases were investigated and these are summarised in Table 1.

3.3. Boswellia species

The species that has undergone most investigation is *B. serrata* with 340 papers referring to this species. In six papers, the species was cited as *B. thurifera* and in one paper as *B. glabra*. Several spelling variations were also seen including *serata* and *serrate*. The second most frequently researched species was *B. sacra* (156 papers). The majority of these papers referred to *Boswellia carteri* rather than *B. sacra*, a synonym for the same species. Other synonyms (*B. bhaw-dajiana*) and spelling variations (*sarca; carterii*) were also used. Other species commonly reported included *B. dalzielli* Hutch. (26 papers), *B. papyrifera* (23 papers) and *Boswellia ovalifoliolata* N.P.Balakr. & A.N.Henry (17 papers). The widest range of species investigated was in the field of Cancer and Neoplasms: extracts and/or products from 11 different species were investigated in *in vitro* studies, fewer in *in vivo* research (7) and only *those from B. serrata* in clinical studies in cancer. Extracts and/or products from 13 different *Boswellia* species have undergone investigation in at least one research study.

The species and/or order was confused in two papers (e.g. reporting that '*serrata* was extracted from *carteri*') while, in seven papers, *B. carteri and B. sacra* were listed as separate species. The species was not reported in the methods for all papers; reference to the species could only be

Table 1

Health categories (target conditions and order of frequency)	No. of papers*	Study type: number of studies*			*Boswellia* species investigated (most frequent in bold)					Other species investigated	Species in clinical studies
		***In vitro* (human cells)**	***In vivo***	**Clinical**	*dalzielii*	*ovalifoliata*	*papyrifera*	*sacra*	*serrata*		
Blood	2	-	2	-				**x**	**x**		
Cancer and neoplasms	152	128 (125) +2 IS	42	4	x	x	x	x	**x**	d, f, n, o, r, s	*serrata*
Cardiovascular	14	8 (6)	7	-				x	**x**		
Congenital disorders	0	-	-	-							
Ear	0	-	-	-							
Eye	1	-	1	-					**x**		
Infection	73	67 (5)	7	-	X	x	x	x	**x**	a, d, e, n, r, s	
Inflammatory and immune system (generic anti-inflammatory effects, rheumatoid arthritis)	132	65 (34) +2 EV	76	4	x	x	x	x	**x**	e	
Injuries and accidents	2	-	-	2					**x**		
Mental health (generic psychology, behaviour, cognitive)	31	3 (0)	26	2	x		x	x	**x**		*serrata*
Metabolic and Endocrine (diabetes, generic metabolic)	18	-	14	4	x	x		x	**x**		
Musculoskeletal (osteoarthritis, generic arthritis, osteoporosis)	39	8 (1)	20	13	x			x	**x**	f	*serrata*
Neurological (generic neurology, Alzheimer's disease, multiple sclerosis, Parkinson's disease, epilepsy)	63	24 (10) +1 IS	30	11			x	x	**x**	e, s	*papyrifera, serrata*
Oral and Gastrointestinal (generic gastrointestinal, liver, colitis, dental, Crohn's)	61	16 (12)	35	11		x	x	x	**x**		*serrata*
Renal and Urogenital (generic renal/urinary, testicular, spermatogenesis)	15	-	13	2			x	x	**x**		*serrata*
Reproductive health and childbirth	5	-	3	2				**x**	**x**		*serrata*
Respiratory (generic respiratory, asthma)	8	1 (0)	5	2			x	x	**x**		*serrata*
Skin	20	10 (6)	4	7			x	x	**x**		*sacra, serrata*
Stroke	1	1 (0)	-	1					**x**		not reported
Generic health relevance											
Anti-oxidant effects	*25*	*19 (3) +1 EV*	*7*		*x*	*x*	*x*	*x*	***x***	*d, e, s*	
Pharmacology	*34*	*28 (12) +1 EV*	*8*		*x*		*x*	*x*	***x***	*e*	
Pharmacokinetics	*35*	*15 (8) +2 EV*	*14*	*9*	*X*		*x*	*X*	***x***	*f*	*serrata*
Toxicology/toxicity	*22*	*6 (5)*	*20*		*X*	*x*	*x*	*x*	***x***		
Prevention of toxicity	*26*	*10 (7)*	*17*			*x*		*x*	***x***		
Disputed Aetiology and Other	1			1					**x**		
Growth & development	*1*		*1*						***x***		
Pain	*15*		*12*	*3*	*X*			*x*	***x***	*e*	*serrata*
Diet, Obesity and Nutrition (obesity)	7	3 (1)	4			x			**x**		

Key EV: *ex vivo*, IS: *in silico*, a: *B. ameero*, d: *B. dioscorides*, e: *B. elongata*, f: *B. frereana*, n: *B. neglecta*, o: *B. occulta*, r: *B. rivae*, s: *B. socotrana*

* numbers of studies may total more than the original numbers of papers as, for example, a study on both anticancer and anti-inflammatory effects was counted in both relevant categories.

found in the introduction in 59. In 88 papers, the species was not reported at all while access could not be obtained to 35 papers.

3.4. Form of Boswellia

A wide range of different forms of *Boswellia* were employed in the studies. Clinical studies were identified that had investigated gum resin or resin extract, boswellic acids or a specific acid, standardised extract, lecithin-based and phytosome-based delivery forms of the extract, solid lipid particles, topical microemulsion, frankincense oil, leaf fractions and essential oils of *B. dalzielli*. In the *in vivo* studies, the forms of *Boswellia* were as per the clinical studies plus incense (smoke produced by burning the resin), semi-synthetic forms of boswellic acids, a homoeopathic form of boswellic acid, stem bark extract (from *B. dalzielli*), analogues of boswellic acids, aqueous and alcoholic extracts, and glycosides. *In vitro* studies focused on various constituents and leaf and bark extract. In addition, different delivery forms were investigated. Overall, of the constituents, the boswellic acids were investigated most frequently: 3- Acetyl-11-keto-β-Boswellic acid (AKBA) was investigated in most studies followed by 11-Keto-β-Boswellic acid (KBA).

4. Most frequently researched categories

4.1. Cancer and Neoplasms

Within the area of cancer, studies of *Boswellia* were most frequent in breast cancer (29 papers); prostate cancer (16); colorectal cancer (16); brain tumours (16); leukaemia (15). The majority of studies focused on anticancer mechanisms or effects (140 papers). Fewer focused on potentiation of anticancer agents (16), prevention of adverse effects of anticancer agents (8) or prevention of cancer (13). Potentiation of anticancer agents was studied in the context of various cancers and included agents such as cisplatin, doxorubicin, epirubicin and temozolomide. Eight studies specifically investigated methods for enhanced delivery of *Boswellia*.

Only four clinical studies were identified and these all addressed brain oedema in brain tumour patients. Small preliminary studies with promising results (e.g. [27]) were followed by a randomised controlled trial in 2011 reporting beneficial effects of *Boswellia* [28]. Subsequently, only a small pilot study was located [29]. No clinical studies in other cancers could be found except for one on prevention of radiotherapy-induced skin damage in breast cancer using a *Boswellia*--based cream [30].

4.2. Inflammatory and immune system

A large number of studies assessed anti-inflammatory effects of *Boswellia*. While 35 of these were in humans or human cells, a significant proportion of this work was in animal cells or *in vivo* (76 studies). Very limited translation into clinical studies was identified, only four studies.

4.3. Infection

A wide range of *Boswellia* species have been tested for effects on infections, the majority being *in vitro* against various organisms. A small number were conducted in animals and no corresponding clinical studies were identified.

5. Generic aspects of *Boswellia*

5.1. Pharmacokinetics

Thirty-five publications reported pharmacokinetic studies that were carried out using a range of techniques: nine were clinical studies, 14 were studies conducted in animals and 15 were *in vitro* studies (several publications reported more than one type of study). The majority of reports related to extracts and/or products originating from *B. serrata*, one reported using an extract of *B. papyrifera* and one tested extracts from various species. The substance being investigated included the pure boswellic acids, which had been obtained from an external supplier, or extracts obtained, in most cases, using ethanol/methanol-based processes. Other studies investigated novel formulations which included nanoparticles, floating microspheres, elastosomes, lecithin delivery forms, phosphotidylcholine complexes and various commercially available capsules. Virtually all studies measured levels of at least one boswellic acid, most frequently AKBA or KBA, with some assessing up to six different boswellic acids. Absorption and distribution including permeation of skin and of the blood brain barrier were amongst the parameters measured.

5.2. Toxicity of Boswellia

A total of 22 publications reported toxicology studies involving *Boswellia*-derived extracts or products. Six were *in vitro* assessments, in five cases using human cells. Twenty *in vivo* studies were located that examined possible toxic effects of *Boswellia* extracts or products. Eighteen studies involved the use of rodents (rats or mice). Several older studies involved rabbits or monkeys although rabbits were also used in one more recent study to test for acute dermal and eye irritation.

The substances being investigated varied, with products or extracts from five species (*B. serrata, B. dalzielli, B. sacra, B ovalifoliata* and *B. papyrifera*). Nearly half of the studies involved an alcoholic extract of the resin (from *B. papyrifera, B.serrata* or *B. sacra*) or the bark (from *B. dalzielli* or *B.ovalifoliata*). Other substances tested included aqueous extracts, a powder, an essential oil and a single boswellic acid (AKBA). Seventeen tests were carried out within 28 days while two were over 90 days and one assessed chronic toxicity over 6 months. The subchronic and chronic tests all involved *B. serrata*-derived products. Acute toxicity tests were carried with several different *B.serrata*-derived extracts or products and those from other species including *B. papyrifera* and *B. dalzielli*. In most cases, either an acute toxicity test was conducted or a generic safety assessment with a panel of different assessments. Studies which had a specific focus included those carrying out an assessment of geno-, haemo-, liver, skin or testicular toxicity.

6. Discussion

It is clear from this scoping study that there has been extensive and sustained investigation of extracts and products derived from *Boswellia* species, primarily *B. serrata* and *B. sacra*. The intention of this study was not to analyse and collate all the results presented which would not be possible due to the large and varied nature of the research and which would require rigorous systematic reviews on each specific topic area. The aim was to provide a clear picture of the research activity to date and some broad generic conclusions have been drawn.

The focus of attention in terms of medical conditions has been on cancer, inflammatory diseases and infections. In the cancer field, while a large number of *in vitro* and animal studies report anticancer activity including inhibition of tumorigenesis and apoptosis of cancer cells, there has limited translation of this activity into clinical studies. As reported by previous authors, such as Efferth and Oesch [21], further randomised controlled trials would be required to confirm or otherwise any anticancer effect. Conversely, in the case of osteoarthritis, the number of clinical studies on osteoarthritis exceeded the number of *in vitro* studies and was only slightly less than the number of animal studies. All involved a control group although treatments were only randomised in seven cases and most reported positive or promising results with a form of *Boswellia*. However, different formulations were used as were different control interventions, both of which may explain the high heterogeneity revealed in a recent systematic review on the topic [22]. The effects of *Boswellia* have been tested on a wide range of infective organisms but no corresponding clinical studies were identified within

this scoping study.

A high proportion of the studies have been carried out in animals, particularly in some areas. For example, large numbers of animal studies appeared in the Inflammation and Immune System category. It is unclear to what extent these have informed clinical studies and this would be potentially important aspect for further inquiry. Investigation of the potential toxicity of *Boswellia* has also been carried out in various animal studies. Further investigation of the extent, if any, of duplication within this set would be valuable in view of the 3Rs initiative to ensure more ethical use of animals in research (NC3Rs) [31]. A preliminary analysis within this scoping study indicates that a range of different extracts and products were tested. Nevertheless, collating this data across toxicity studies would also provide more reliable evidence to inform any future clinical research. While this has been carried out by some authors, for example Efferth and Oesch [21] collated 9 studies up to 2016, further work on this aspect is required as this scoping study identified at least 10 relevant studies published since 2019.

Many of the recognised *Boswellia* species have been studied, with *B. serrata* and *B. sacra* receiving most attention. While few examples of explicit misnaming or confusion over species were encountered, it was apparent that reporting could be improved in a number of cases. In some papers, lists of species included synonyms for the same species while in some papers no reference was made to species. Improving the reporting will require that authors consult international sources to confirm accepted names and adhere to recommendations on accurate scientific nomenclature for plants [32]. In the case of cancer and infections, research has focused on a range of species and some of the species most frequently researched have been classified as vulnerable with populations decreasing (e.g. *B. ovalifoliolata*) or near threatened (e.g. *B. sacra*) [3]. Consideration of sustainability is relevant to planning of future research in this area.

The range of constituents and forms investigated provides further diversity and complicates interpretation of results on possible effects of *Boswellia*. Formulations including nanoparticles and phytosomes as well as various derivatives have been tested. It is clear that delivery of *Boswellia* and its active constituents, particularly the boswellic acids, continues to provide a challenge to any attempt to use these agents clinically. Learning from experience gained within one area or for one medical condition on such generic aspects of *Boswellia* therapy would be valuable to other areas or conditions and it is vital that findings from such research are identified and applied widely.

7. Limitations

Limitations of this scoping study include the fact that the majority of the categorisation was carried out by one researcher although sampling of this process was carried out by a second researcher. The full-text of a number of papers could not be retrieved, either due to inaccessibility of the journal or to resource constraints. However, this was a small proportion of the total number and relevant details were extracted from the abstracts. In addition, this study focused on studies published in English in order that methods used and details of the *Boswellia* investigated could be extracted by the authors. Finally, it was not possible within the resources for this scoping study to include full details of the extracts and methods of extraction, and formulation of the specific products tested in the original studies. Even if this data had been collected, it would not have been possible to summarise this information in a meaningful way due to the number of studies and scope in the types of studies, conditions, timescales etc. that were located. It is for this reason that we suggest that further analysis of specific areas is required. We have, however, carried out a more detailed analysis of studies within two areas, pharmacokinetics and toxicity, in an effort to demonstrate the complexity of the information and the range of studies that have been conducted (see relevant sections).

8. Conclusions

This scoping study aimed to reveal the extent and scope of research that has been conducted on the effects of *Boswellia*-derived extracts and products in medicine and health. It provides a clear picture of the range of species from which the investigated substances have been derived and the conditions which have proved the main focus of research efforts. It also highlights research which may have more widely applicable results, for example that on pharmacokinetics, delivery and toxicity. Additionally, the study provides an indication of the current research gaps in this area and highlights the need for accurate reporting of plant material in research. The results should inform future research efforts in this area including potential targets for greater collation of existing data to reduce duplication.

CRediT authorship contribution statement

Karen Pilkington: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Funding acquisition. **Geoffrey John Pilkington:** Conceptualization, Methodology, Validation, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Financial support

This study (and KPs time) was funded by Animal Free Research UK. The funding was unrestricted and the funders had no input to the design, conduct or reporting of the research.

Acknowledgments

The authors are grateful for the support of the Animal Free Research UK charity in supporting this research.

Data availability

The datasets used and/or analysed during the study are available from the corresponding author upon reasonable request.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eujim.2022.102197.

References

[1] Royal Botanic Garden Kew Plants of the World Online. Boswellia Roxb. ex Colebr. https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:5117-1) (Accessed 12th April 2022).
[2] A. Moussaieff, R. Mechoulam, *Boswellia* resin: from religious ceremonies to medical uses; a review of *in-vitro, in-vivo* and clinical trials, J. Pharm. Pharmacol. 61 (10) (2009) 1281–1293, https://doi.org/10.1211/jpp/61.10.0003.
[3] International Union for Conservation of Nature (IUCN) 2022. The IUCN red list of threatened species. Version 2022-1. https://www.iucnredlist.org. (Accessed 9th September 2022).
[4] F. Bongers, P. Groenendijk, T. Bekele, et al., Frankincense in peril, Nat. Sustain. 2 (2019) 602–610, https://doi.org/10.1038/s41893-019-0322-2.
[5] J.A. Duke, CRC Handbook of Medicinal Spices, CRC Press, London, 2019. ISBN 9780367395766.
[6] A. Al-Harrasi, A.L. Khan, S. Asaf, A. Al-Rawahi, Taxonomy, distribution and ecology of *Boswellia*. Biology of Genus Boswellia, Springer, Cham, 2019, pp. 11–34, https://doi.org/10.1007/978-3-030-16725-7_2, pAccessed 14th April 2022.
[7] C.A. Michie, E. Cooper, Frankincense and myrrh as remedies in children, J. R. Soc. Med. 84 (10) (1991) 602–605.

[8] C.L. Woolley, M.M. Suhail, B.L. Smith, K.E. Boren, L.C. Taylor, M.F. Schreuder, J. K. Chai, H. Casabianca, S. Haq, H.K. Lin, A.A. Al-Shahri, S. Al-Hatmi, D.G. Young, Chemical differentiation of *Boswellia sacra* and *Boswellia carterii* essential oils by gas chromatography and chiral gas chromatography-mass spectrometry, J. Chromatogr. A 1261 (2012) 158–163, https://doi.org/10.1016/j.chroma.2012.06.073.

[9] T. Glaser, S. Winter, P. Groscurth, H. Safayhi, E.R. Sailer, H.P. Ammon, M. Schabet, M. Weller, Boswellic acids and malignant glioma: induction of apoptosis but no modulation of drug sensitivity, Br. J. Cancer 80 (5-6) (1999) 756–765, https://doi.org/10.1038/sj.bjc.6690419.

[10] Y. Jing, S. Nakajo, L. Xia, K. Nakaya, Q. Fang, S. Waxman, R. Han, Boswellic acid acetate induces differentiation and apoptosis in leukemia cell lines, Leuk. Res. 23 (1) (1999) 43–50, https://doi.org/10.1016/s0145-2126(98)00096-4.

[11] T. Syrovets, J.E. Gschwend, B. Büchele, Y. Laumonnier, W. Zugmaier, F. Genze, T. Simmet, Inhibition of IkappaB kinase activity by acetyl-boswellic acids promotes apoptosis in androgen-independent PC-3 prostate cancer cells *in vitro* and *in vivo*, J. Biol. Chem. 280 (7) (2005) 6170–6180, https://doi.org/10.1074/jbc.M409477200.

[12] J.J. Liu, B. Huang, S.C. Hooi, Acetyl-keto-beta-boswellic acid inhibits cellular proliferation through a p21-dependent pathway in colon cancer cells, Br. J. Pharmacol. 148 (8) (2006) 1099–1107, https://doi.org/10.1038/sj.bjp.0706817.

[13] K.G. Byler, W.N. Setzer, Protein targets of frankincense: a reverse docking analysis of terpenoids from *Boswellia* oleo-gum resins, Medicines 5 (3) (2018) 96, https://doi.org/10.3390/medicines5030096 (Basel).

[14] U. Siemoneit, A. Koeberle, A. Rossi, F. Dehm, M. Verhoff, S. Reckel, T.J. Maier, J. Jauch, H. Northoff, F Bernhard, V. Doetsch, L. Sautebin, O. Werz, Inhibition of microsomal prostaglandin E2 synthase-1 as a molecular basis for the anti-inflammatory actions of boswellic acids from frankincense, Br. J. Pharmacol. 162 (1) (2011) 147–162, https://doi.org/10.1111/j.1476-5381.2010.01020.x.

[15] H.P. Ammon, Boswellic acids and their role in chronic inflammatory diseases, Adv. Exp. Med. Biol. 928 (2016) 291–327, https://doi.org/10.1007/978-3-319-41334-1_13.

[16] N.K. Roy, D. Parama, K. Banik, D. Bordoloi, A.K. Devi, K.K. Thakur, G. Padmavathi, M. Shakibaei, L. Fan, G. Sethi, A.B. Kunnumakkara, An update on pharmacological potential of boswellic acids against chronic diseases, Int. J. Mol. Sci. 20 (17) (2019) 4101, https://doi.org/10.3390/ijms20174101.

[17] K. Huang, Y. Chen, K. Liang, X. Xu, J. Jiang, M. Liu, F. Zhou, Review of the chemical composition, pharmacological effects, pharmacokinetics, and quality control of *Boswellia carterii*, Evid. Based Complement. Alternat. Med. 2022 (2022), 6627104, https://doi.org/10.1155/2022/6627104.

[18] M. Miran, K. Amirshahrokhi, Y. Ajanii, R. Zadali, M.W. Rutter, A. Enayati, F. Movahedzadeh, Taxonomical investigation, chemical composition, traditional use in medicine, and pharmacological activities of *boswellia sacra* flueck, Evid. Based Complement. Alternat. Med. 2022 (2022), 8779676, https://doi.org/10.1155/2022/8779676.

[19] M. Khajehdehi, M. Khalaj-Kondori, B. Baradaran, Molecular evidences on anti-inflammatory, anticancer, and memory-boosting effects of frankincense, Phytother. Res. (2022) 10, https://doi.org/10.1002/ptr.7399. Online ahead of print.

[20] H. Hussain, I. Ali, D. Wang, F.L. Hakkim, B. Westermann, L. Rashan, I. Ahmed, I. R. Green, Boswellic acids: privileged structures to develop lead compounds for anticancer drug discovery, Expert Opin. Drug Discov. 16 (8) (2021) 851–867, https://doi.org/10.1080/17460441.2021.1892640.

[21] T. Efferth, F. Oesch, Anti-inflammatory and anti-cancer activities of frankincense: targets, treatments and toxicities, Semin. Cancer Biol. 80 (2022) 39–57, https://doi.org/10.1016/j.semcancer.2020.01.015.

[22] G. Yu, W. Xiang, T. Zhang, L. Zeng, K. Yang, J. Li, Effectiveness of *Boswellia* and *Boswellia* extract for osteoarthritis patients: a systematic review and meta-analysis, BMC Complement. Med. Ther. 20 (1) (2020) 225, https://doi.org/10.1186/s12906-020-02985-6.

[23] A. Siddiqui, Z. Shah, R.N. Jahan, I. Othman, Y. Kumari, Mechanistic role of boswellic acids in Alzheimer's disease: emphasis on anti-inflammatory properties, Biomed. Pharmacother. 144 (2021), 112250, https://doi.org/10.1016/j.biopha.2021.112250.

[24] A.A. Gomaa, H.S. Mohamed, R.B. Abd-Ellatief, M.A. Gomaa, Boswellic acids/ *Boswellia serrata* extract as a potential COVID-19 therapeutic agent in the elderly, Inflammopharmacology 29 (4) (2021) 1033–1048, https://doi.org/10.1007/s10787-021-00841-8.

[25] H. Arksey, L. O'Malley, Scoping studies: towards a methodological framework, Int. J. Soc. Res. Methodol. 8 (1) (2005) 19–32, https://doi.org/10.1080/1364557032000119616.

[26] UKCRC (UK Clinical Research Collaboration) Health research classification system. Health categories. HRC Online. https://hrcsonline.net/health-categories/. (Accessed 14th April 2022).

[27] J.R. Streffer, M. Bitzer, M. Schabet, J. Dichgans, M. Weller, Response of radiochemotherapy-associated cerebral edema to a phytotherapeutic agent, H15, Neurology 56 (9) (2001) 1219–1221.

[28] S. Kirste, M. Treier, S.J. Wehrle, G. Becker, M. Abdel-Tawab, K. Gerbeth, M.J. Hug, B. Lubrich, A.L. Grosu, F. Momm, *Boswellia serrata* acts on cerebral edema in patients irradiated for brain tumors: a prospective, randomized, placebo-controlled, double-blind pilot trial, Cancer 117 (16) (2011) 3788–3795, https://doi.org/10.1002/cncr.25945.

[29] F. Di Pierro, G. Simonetti, A. Petruzzi, A. Bertuccioli, L. Botta, M.G. Bruzzone, V. Cuccarini, L. Fariselli, E. Lamperti, A novel lecithin-based delivery form of Boswellic acids as complementary treatment of radiochemotherapy-induced cerebral edema in patients with glioblastoma multiforme: a longitudinal pilot experience, J. Neurosurg. Sci. 63 (3) (2019) 286–291, https://doi.org/10.23736/S0390-5616.19.04662-9.

[30] S. Togni, G. Maramaldi, A. Bonetta, L. Giacomelli, F. Di Pierro, Clinical evaluation of safety and efficacy of *Boswellia*-based cream for prevention of adjuvant radiotherapy skin damage in mammary carcinoma: a randomized placebo controlled trial, Eur. Rev. Med. Pharmacol. Sci. 19 (8) (2015) 1338–1344.

[31] National Centre for the Replacement, Refinement and reduction of animals in research (NC3Rs). The 3Rs. Available at: https://nc3rs.org.uk/who-we-are/3rs. Accessed 27th April 2022.

[32] D. Rivera, R. Allkin, C. Obón, F. Alcaraz, R. Verpoorte, M. Heinrich, What is in a name? The need for accurate scientific nomenclature for plants, J. Ethnopharmacol. 152 (3) (2014) 393–402. Mar 28.