** INTRODUCTION **

Review question / Objective: A systematic review of the literature was carried out to summarize the phenolic compounds and bioactive properties identified in C. album berries and leaves and search for research gaps on this topic.

Rationale: The berries from the Corema album have been employed in popular medicine since ancient times and nowadays, gained increased attention as a natural source as natural medicinal agents. More recently the composition of berries and leaves of C. album has been studied concerning their chemical compositions,
content in phenolic derivatives, and bioactive properties. A summary of phenolic compounds and bioactive properties identified in C. album berries and leaves will evidence the research gaps on this topic that need further studies.

Condition being studied: Summarize the phenolic compound's composition of Corema album berries and leaves assessed by advanced analytical methods and assessment of their bioactive properties.

METHODS

Search strategy: PRISMA methodology was applied by performing a search for publications in three databases PubMed, SCOPUS, and Web of Science using the following keywords: (“Corema album” AND (berries OR leaves)). The collection of papers was done up to Jun 15th, 2022. A total of 74 publications were identified after compiling all three databases. Duplicates, reviews and opinion articles (n=39) were removed.

Participant or population: This systematic review does not involve patients, participants or population, only chemical analyses and in vitro assays.

Intervention: Not applicable.

Comparator: Not applicable.

Study designs to be included: Phenolic compounds composition of Corema album berries, leaves, and extracts assessed by chemical analyses and advanced analytical methods. Their bioactive properties have been studied by in vitro assays.

Eligibility criteria: Studies focused on chemical composition of berries, leaves, or their extract and their bioactive properties. Exclusion criteria: agronomic and archaeological studies.

Information sources: Three databases PubMed, SCOPUS, and Web of Science as information sources. The following keywords were used: (“Corema album” AND (berries OR leaves)). Contact with authors or grey literature was not used as information source.

Main outcome(s): Although a wide variety of phenolic compounds have been identified in berries and leaves from C. album, up to the date of this review (Jun 15th, 2022), there is scarce scientific data regarding the potential health benefits exerted by C. album. Only 9 studies evaluated the biological properties of berries or leaves of this plant. All those studies were in vitro cell assays. Nevertheless, the discussion section evidences that their rich composition in phenolic compounds is promising concerning health benefits and therapeutic potential. The phenolic compounds identified in C. album leaves and berries can modulate several pathophysiological processes, namely inflammation, oxidative stress, carcinogenesis, etc., this plant can also be attractive to the pharmaceutical industry to generate new drug(s), nutraceuticals, or supplements. Nevertheless, scientific evidence concerning C. album bioactivity is still required.

Data management: Data obtained from the three databases (PubMed, SCOPUS, and Web of Science) up to Jun 15th, 2022, using the keywords: (“Corema album” AND (berries OR leaves)) was exported to excel, and merged. Duplicates, reviews and opinion articles were removed. Two authors of this publication screened independently the title and abstract of the remained articles. Inclusion and exclusion criteria was applied. Then, the full text of eligible articles was carefully studied by all authors and data concerning phenolic compounds identified, C. album samples (berries, leaves, extracts) and bioactive properties studied was collected. In all steps, disagreements were solved by meeting all authors and deciding together the inclusion or exclusion of the articles.

Quality assessment / Risk of bias analysis: The quality of the methodologies used for the identification of phenolic compounds in C. album was assessed. Only studies that apply advanced methodologies were
considered, while those that undertake only the quantification of total phenolic content were not considered. Concerning in vitro cell assays it was confirmed that they follow good practices for in vitro cell methods.

**Strategy of data synthesis:** Both berries and leaves from C. album revealed a rich content in several phenolic compounds, which were summarized in Tables. The phenolic compounds were divided into three main groups, phenolic acids, flavonoids and stil-benes, according to their structural similarities. The bioactive properties of both berries and leaves from C. album were summarized in a Figure.

**Subgroup analysis:** Two sub-groups were divided, the studies done with berries and those done with leaves.

**Sensitivity analysis:** Sensitivity analysis was done by confirming that the bioactivity assessed in C. album berries or leaves was linked with phenolic compounds composition.

**Language restriction:** English and Portugueses.

**Country(ies) involved:** Portugal.

**Keywords:** Corema album; berries; leaves.

**Dissemination plans:** Publication in an international scientific journal.

**Contributions of each author:**
Author 1 - Ana Sofia Cerquido - original draft preparation, writing—review and editing.
Email: anacerquido99@gmail.com
Author 2 - Martin Vojtek - Conceptualization, original draft preparation, writing—review and editing.
Email: matovoj@gmail.com
Author 3 - Rita Ribeiro-Oliveira - Conceptualization, writing—review and editing, original draft preparation.
Email: rita_rmo@hotmail.com
Author 4 - Olga Viegas - Independent publication screening, data management, original draft preparation and feedback.
Email: olgaviegas@fcna.up.pt
Author 5 - Joana Beatriz Sousa - Conceptualization, writing—review, editing, and approved.
Email: jbsousa@ff.up.pt
Author 6 - Isabel M.P.L.V.O. Ferreira - Conceptualization, funding acquisition, independent publication screened, data management, read, provided feedback and approved.
Email: isabel.ferreira@ff.up.pt
Author 7 - Carmen Diniz - Conceptualization, funding acquisition, original draft preparation, writing—review and editing and approved.
Email: cdiniz@ff.up.pt