

INPLASY

A Systematic Review Of Chemical Compounds With Immunomodulatory Action Isolated From African Medicinal Plants

INPLASY202410116

doi: 10.37766/inplasy2024.1.0116

Received: 28 January 2024

Published: 28 January 2024

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ADMINISTRATIVE INFORMATION

Support - Laboratoire de développement du médicament/ CEA CFORUM.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202410116

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 January 2024 and was last updated on 28 January 2024.

INTRODUCTION

Review question / Objective How have immunomodulatory activities of molecules isolated from African medicinal plants been assessed, and what are the proposed mechanisms based on molecular action?

Rationale Traditional medicine in Africa is the cornerstone of the health system. Populations use medicinal plants to fight various diseases, especially infectious and inflammatory ones. The immune system comprises a complex network of cells and biological mediators that safeguard the body against harm from foreign invaders like microbes and malignant cell infiltration while preventing excessive immune activation. The innate and adaptive immunities work synergistically to protect the body[7]. Several endogenous and exogenous factors may influence

the immune system's effectiveness, potentially leading to malfunction. Pandemic or epidemic diseases such as COVID-19, dengue fever, and autoimmune diseases correspond to an inappropriate immune response [5,8,9]. Cytokine storms (involving IL1 β , IL6, and Tumor Necrosis Factor α) exacerbate these diseases [3,8]. Also, in autoimmune diseases, self-reactive T cells and exaggerated production of antibodies against the body's tissues result in persistent inflammation[2]. Control the immune response by modification of induction, expression, amplification, or inhibition of a part or phase of the immune response[3,4], referred to as immunomodulation of body defense. Synthetic immunomodulatory drugs are used in therapy but have adverse effects and a broad impact on the entire immune system, constitute a limit to the extended use of these drugs, and justify the search for more effective and safe agents with targeted immunomodulatory activity. Previous

studies have shown that natural products with immunomodulatory activity have already been used to treat autoimmune diseases, inflammatory disorders, cancer, and infectious diseases (dengue fever, COVID-19)[1]. These substances constitute a valuable source of biologically active secondary metabolites, including alkaloids, flavonoids, coumarins, glycosides, polysaccharides, phenols, terpenes, and terpenoids. However, much remains to be done to find safe and effective molecules. Today's research focuses on identifying molecules that modulate gene transcription pathways to control the immune system. Knowledge of chemical structures will allow the optimization of structure-activity relationships.

The research question of this review is: How have immunomodulatory activities of molecules isolated from African medicinal plants been assessed, and what are the proposed mechanisms based on molecular action? Analyzing gathered knowledge will allow understanding the mechanism of action of immunomodulatory properties of chemicals isolated from African medicinal plants, which can yield new therapeutic indications.

Condition being studied African medicinal plants yield effectiveness on various pathologies such as infectious, inflammatory, and cancer diseases. We will explore those that were already studied with isolated chemical compounds. Used experimental models and convergent mechanisms of action of those chemicals will be highlighted.

METHODS

Search strategy The research will be conducted according to PRISMA guidelines [6] to identify studies on African medicinal plants used for their immunomodulatory properties. This exploration will use the scholarly search engine Google Scholar and a comprehensive screening of prominent international databases, including PubMed, ScienceDirect, African Journal Online, and Embase. Our search queries will incorporate specific keywords such as "immunomodulator" OR "immunity" AND "medicinal plant" OR "herbal plant" AND "phytochemicals". The African pharmacopeia and google scholar search motor will be then screened to retained african medicinal plants.

Participant or population African medicinal plants from which chemicals were isolated with the proof of in vivo or in vitro modulation of immune system will be considered.

Intervention Not applicable.

Comparator Not applicable. The analyse will be narrative.

Study designs to be included The review will addressed to studies which preceded to plant identification, extract preparation, chemicals isolation with wholly or partial structure identification, biological effects assessment of immune system modulation and outcomes interpretation.

Eligibility criteria Selection CriteriaWe will consider exclusively: - free access to full-text scientific research articles published in English until the 30th September 2023, - articles whose titles or abstracts focused on the immunomodulatory effects of African medicinal plant chemicals, - The active chemicals involved must be wholly or partially isolated, coupled with subsequent chemical structure determination.We will exclude: - report or grey literature will not be considered (conferences, thesis...),- duplicate (The papers published in two journals with the same title, same first author, same study design, and the same number of in-text citations or references were referred to as duplicate papers),- only available abstracts,- study on total extracts only,- studies with no results based on immunomodulatory activity,- studies not published in English, - And review articles.

Information sources The data will be purchased from scholarly search engine Google Scholar and a comprehensive screening of prominent international databases, including PubMed, ScienceDirect, African Journal Online, and Embase.

Main outcome(s) The outcomes will determine African medicinal plants that undergo bioactive compound structure determination and which yield immunomodulatory properties. The chemical structure, bioactive molecule group, and the biological effects' type and importance will be synthesized.

We will describe the interpretation of mechanism-based action and summarize the convergent mechanism to highlight the immunomodulatory properties.

Additional outcome(s) A chemical structure of bioactive molecules will be reproduced using Chem Draw (version 12.0.1076), and convergent and distinctive signaling pathways will be summarized on a schema.

Data management The data to be collected from each publication include scientific names,

botanical families, used parts of plants, extraction solvents, phytochemical groups, isolated compounds, experimental models for objectifying immunomodulatory activities, obtained results, and the main mechanisms of the isolated compounds. A standardized Excel form will be used to register data. the entries will be : Plants data (species, used parts) type of extract and identified chemical, Investigation models (Animals, Cell lines, Tissues ...) Tested dose (effective Dose/concentration), Methods of analysis or measurement Biologic effects (type, significance) - Mechanism of action and References.

Quality assessment / Risk of bias analysis Two independent evaluators will assess the quality of the extracted data. Some results, such as grey literature and cost-charged access to full-text articles, may need to be included. The difficulties in evaluating the effectiveness of chemical compounds without determining IC50, EC50, or ED50 values and non-significant outcomes will not be considered.

Strategy of data synthesis The final analysis will be narrative, focusing on articles containing phytochemical compounds isolated from African medicinal plants and whose immunomodulatory activity was studied. Two independent evaluators will assess the quality of the extracted data. The chemical structures of the isolated compounds will be generated using Chem Draw (version 12.0.1076), and convergent and distinctive signaling pathways will be summarized.

Subgroup analysis Data will be described according to the chemical group.

Sensitivity analysis It is not applicable as the analysis of outcomes will be narrative.

Language restriction The data will be extracted from articles published in English language.

Country(ies) involved Lectures, searchers and Ph.D students of Universite Joseph KI-ZERBO and Universite NAZI Boni Univer from Burkina Faso in West Africa conducted the study.

Other relevant information The systematic review is a part of the Ph.D. research project of Arsene NIKIEMA, a CEA-CFOREM fellow.

Keywords African medicinal plants ; Phytochemicals ; Immunomodulators ; Transduction.

Dissemination plans The outcomes of the systematic review will be published in a review article and will constitute a part of the Ph.D. thesis dissertation of NIKIEMA Arsène.

Contributions of each author

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