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**Keywords:** Plant secondary metabolites, Vaccine, Adjuvants, Immunomodulation, Africa.

**Abstract:**

**Abstract:** Plant secondary metabolites constitute a chemically diverse group of natural products that exert immunomodulatory and adjuvant activities and may complement conventional vaccine technologies and inform regionally appropriate vaccine strategies in Africa. A structured narrative review of English-language literature published from 2000 through 2025 was performed using PubMed, Google Scholar, Elsevier and EBSCOhost. Search terms combined descriptors for plant secondary metabolites, saponin, adjuvant, vaccine, immunomodulator, Africa and nanoformulation. Inclusion criteria comprised original research articles, systematic reviews and clinical trial reports addressing mechanisms of action, formulation science, safety and clinical development; exclusion criteria comprised non-English reports, conference abstracts without full text and studies lacking primary data. Evidence was categorized by study type: in vitro experiments, animal models, formulation and stability studies, and human clinical investigations. Preclinical data indicate that selected plant secondary metabolites enhance antigen presentation, promote dendritic cell maturation and potentiate both humoral and cell-mediated immune responses through modulation of nuclear factor kappa B signalling, mitogen-activated protein kinase cascades, phosphatidylinositol 3-kinase/protein kinase B pathways and toll-like receptor signalling. Purified triterpenoid saponin fractions derived from *Quillaja saponaria* have been formulated within liposomal adjuvant systems and incorporated into adjuvant platforms that have progressed from phase I to phase III clinical evaluation; other saponin-enriched preparations have completed phase I or phase II studies. Polysaccharide fractions, including arabinogalactans isolated from *Moringa oleifera*, and defined flavonoids from *Curcuma longa* and *Artemisia annua* produce reproducible immunostimulatory effects in animal models and enhance antigen stability in formulation studies. Encapsulation within biodegradable polymeric matrices and mucoadhesive carriers improves protection of labile compounds and facilitates mucosal and transdermal delivery in preclinical systems; however, clinical validation of extended shelf life and operational stability under field conditions remains limited. Safety and tolerability are compound- and formulation-dependent; standardized phytochemical characterization, contaminant screening and comprehensive toxicological assessment are prerequisites for clinical translation. Establishing safety and efficacy in target populations will require regulatory harmonization, validated manufacturing and quality-control processes, and adequately powered, hypothesis-driven clinical trials with predefined immunological and clinical endpoints.

## Declarations

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*Contribution:* Conceptualization, Formal analysis, Methodology, Supervision.

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### Conflict of Interest

The authors declare no conflicting interest.

### Data Availability

Publicly available

### Ethics Statement

Not applicable

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## References

## Additional Information

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