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Review Article

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Bioactive Compounds from African Medicinal Plants in Ulcerative Colitis: Mechanistic Insights and Therapeutic Prospects -A Narrative Review

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ABSTRACT

Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease that primarily affects the rectum and colon. Despite the availability of standard therapies, many patients fail to achieve sustained remission, and current treatments are often associated with significant adverse effects, high costs, and limited accessibility particularly in resource-constrained regions such as Africa. The pathogenesis of UC is multifactorial, involving a complex interplay of genetic predisposition, environmental insults, epithelial barrier dysfunction, immune dysregulation, and persistent oxidative stress. African traditional medicine provides a rich repository of medicinal plants historically employed in the management of gastrointestinal disorders, and growing preclinical evidence supports their therapeutic potential. For example, Alstonia boonei extracts have demonstrated potent anti-colitic activity by attenuating pro-inflammatory cytokines and oxidative stress markers, with effects comparable to or exceeding certain conventional treatments. Other plants of ethnomedicinal relevance, including Aloe barbadensis, Vernonia amygdalina, and Azadirachta indica, contain diverse bioactive constituents such as flavonoids, terpenoids, and alkaloids. These compounds exert anti-colitic effects through mechanisms including inhibition of NF-κB signaling, suppression of COX-2 expression, antioxidant defense enhancement, and immunomodulatory modulation. While extensive traditional knowledge exists, rigorous scientific validation remains insufficient. Further investigations are required to elucidate mechanisms of action, confirm efficacy, and establish safety profiles. Bridging traditional knowledge with modern pharmacological research holds promise for developing accessible, affordable, and culturally acceptable complementary therapies to address the unmet needs of UC patients worldwide.

Keywords: Ulcerative Colitis, African Medicinal Plants, Traditional Medicine, Anti-Inflammatory, Bioactive Compounds, Ethnobotany, Pathophysiology, Alternative Therapy, Oxidative Stress

List of Abbreviations

COX-2	:	Cyclooxygenase-2
DSS	:	Dextran Sodium Sulfate
GI	:	Gastrointestinal
HMPL-004	:	A code for a specific herbal extract (Andrographis paniculata)
IBD	:	Inflammatory Bowel Disease
IL-1β	:	Interleukin-1 beta
IL-6	:	Interleukin-6
IL-13	:	Interleukin-13
IL-17	:	Interleukin-17
JAK	:	Janus Kinase
JAMs	:	Junctional Adhesion Molecules
MUC2	:	Mucin 2
NF-κB	:	Nuclear Factor kappa-light-chain-enhancer of activated B cells
PPAR-γ	:	Peroxisome Proliferator-Activated Receptor gamma
PGE_2	:	Prostaglandin E2
ROS	:	Reactive Oxygen Species

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STAT6	:	Signal Transducer and Activator of Transcription 6
Th1	:	T-helper 1 cell
Th2	:	T-helper 2 cell
Th17	:	T-helper 17 cell
TNF-α	:	Tumour Necrosis Factor-alpha
TNBS	:	2,4,6-Trinitrobenzenesulfonic Acid
UC	:	Ulcerative Colitis

Introduction

Ulcerative Colitis: Overview and Pathogenesis

Ulcerative colitis (UC) is a chronic, relapsing inflammatory bowel disease (IBD) primarily affecting the rectum and colon. The condition is most commonly diagnosed between 30 and 40 years of age. UC is characterized by continuous mucosal inflammation that originates in the rectum and extends proximally through the colon, leading to clinical manifestations such as abdominal pain, chronic bloody diarrhea, and systemic symptoms including weight loss and fever [1-3].

The pathogenesis of UC involves a complex interplay of genetic susceptibility, environmental factors, epithelial barrier dysfunction, and dysregulated immune responses. These processes collectively promote the excessive release of pro-inflammatory cytokines, including interleukin 1β (IL 1β), IL 6, IL 13, and tumor necrosis factor α (TNF α), neutrophil activation, and heightened oxidative stress, culminating in mucosal injury and sustained inflammation [3].

Historically more prevalent in Western populations, UC incidence is rising in developing regions, including parts of Africa. A recent African scoping review of IBD (November 2024) analyzed data from over 7,900 UC patients worldwide and identified an upward trend linked to urbanization, dietary shifts, and improved diagnostic capacity [4].

Despite advances in symptom management through 5-aminosalicylic acid, corticosteroids, immunomodulators, and biologic therapies, long-term remission remains elusive for many patients. Refractory immune activity, drug resistance, adverse effects, and complications such as colorectal cancer or toxic megacolon highlight the pressing need for novel and more effective therapeutic strategies [4].

The Need for Alternative Therapy

urrent management of ulcerative colitis (UC) typically begins with 5-aminosalicylic acid (mesalamine) for mild-to-moderate disease, progressing to corticosteroids, immunosuppressants such as azathioprine, calcineurin inhibitors, and advanced biologics including anti–tumor necrosis factor (TNF) agents (infliximab, adalimumab), integrin antagonists (vedolizumab), and Janus kinase (JAK) inhibitors (tofacitinib), depending on treatment response and disease severity. Although these therapies have improved outcomes, they remain limited by significant drawbacks. Adverse effects such as osteoporosis, metabolic disturbances, hepatotoxicity, heightened infection risk, and the development of immunogenic resistance often complicate long-term use. In addition, the high cost of biologics severely restricts accessibility in low-resource settings [1,5].

Even with optimized regimens, response rates remain suboptimal. Approximately half of patients achieve sustained remission on mesalamine, while others eventually lose responsiveness or fail to respond to newer biologics and targeted therapies. In Sub-Saharan Africa, these challenges are magnified by systemic barriers, including inadequate specialist care, limited diagnostic infrastructure, and prohibitive treatment costs, resulting in delayed diagnosis and suboptimal disease control. These realities underscore the urgent need for widely available, safe, and affordable alternative or adjunct therapeutic options [4,6].

Emerging evidence supports the potential of herbal and plant-derived therapies in UC management. A systematic review of randomized controlled trials reported moderate efficacy for interventions such as tormentil, aloe vera gel, curcumin, butyrate, and wheatgrass juice in inducing remission and improving clinical outcomes. Furthermore, clinical evaluation of andrographolide, a diterpenoid lactone from Andrographis paniculata (HMPL-004), has demonstrated promising efficacy in mild-to-moderate UC, with mucosal healing rates comparable to mesalamine in some studies [7,8].

Given their low toxicity, cultural acceptability, cost-effectiveness, and therapeutic potential, herbal medicines including African traditional medicinal plants warrant critical consideration as adjuncts or alternatives to standard UC therapies, particularly within resource-limited contexts.

Importance of Traditional African Medicine as a Source of Novel Therapy

Africa possesses one of the world's richest repositories of ethnobotanical knowledge, with hundreds of plant species traditionally employed in the management of gastrointestinal disorders. A systematic review of African medicinal plants used against gastric ulcers and Helicobacter pylori identified 360 species across 107 literature sources; however, only about 11% have been scientifically investigated using in vitro or in vivo approaches, underscoring both the wealth of heritage knowledge and the vast untapped research potential. Notably, Hibiscus sabdariffa L. calyx and Terminalia macroptera root demonstrated potent antimicrobial activity (MIC 0.01–0.03 mg/mL), while Piper longum essential oil and Pachira aquatica exhibited remarkable anti-H. pylori activity (MIC 0.01–0.02 mg/mL) [9].

Emerging preclinical evidence also supports the potential application of African medicinal plants in ulcerative colitis (UC). For example, aqueous and methanolic extracts of Alstonia boonei stem bark, a plant traditionally used in Cameroon, were evaluated in dextran sulfate sodium (DSS)-induced colitis in Wistar rats. The extracts significantly reduced pro-inflammatory cytokines (TNF-α, IL-6, IL-1β, PGE_2) and oxidative stress markers (malondialdehyde, nitric oxide), while enhancing antioxidant defense systems (superoxide dismutase, catalase, glutathione). Remarkably, these effects surpassed those of prednisolone (4 mg/kg), demonstrating strong anti-colitic efficacy in a well-established animal model [10].

These findings highlight the vast but underexplored potential of African traditional medicine as a source of novel therapies. Bridging traditional knowledge with rigorous scientific

validation could lead to the development of treatments that are not only effective, but also affordable and culturally acceptable. Such an interdisciplinary approach is particularly critical in Africa, where access to conventional UC therapies remains limited and often prohibitively expensive.

Pathophysiology of Ulcerative Colitis

Barrier Dysfunction & Genetic Susceptibility

The integrity of the colonic epithelial barrier is fundamental to gut health but is markedly compromised in ulcerative colitis (UC). Tight junctions, which regulate selective permeability between intestinal epithelial cells, are composed of proteins such as occludin, claudins, tricellulin, and junctional adhesion molecules (JAMs). In UC, loss or downregulation of these proteins particularly tricellulin has been reported, resulting in increased paracellular permeability and uncontrolled translocation of luminal antigens into the lamina propria. This disruption facilitates persistent immune activation and chronic inflammation.

Genetic susceptibility further contributes to barrier dysfunction. Mutations in the MUC2 gene, which encodes the major mucin responsible for mucus layer formation, lead to defective mucus production and compromised mucosal protection. This loss of barrier defense exacerbates epithelial vulnerability and amplifies inflammatory responses, thereby accelerating UC pathogenesis [11-13].

Immunological Dysregulation & Microbiome Triggers

Disruption of epithelial barrier integrity in ulcerative colitis (UC) permits the translocation of luminal antigens into the lamina propria, where they activate antigen-presenting cells such as dendritic cells and macrophages. These cells release pro-inflammatory cytokines, including interleukin (IL)-1β, IL-6, and tumor necrosis factor-α (TNF-α), amplifying mucosal inflammation. UC is predominantly associated with aberrant T-helper type 2 (Th2) immune responses. Notably, IL-13 promotes epithelial cell apoptosis and tight junction disassembly, thereby exacerbating barrier dysfunction. Furthermore, IL-13 signaling induces STAT6 phosphorylation, while inhibition of STAT6 has been shown to abolish IL-13–mediated apoptosis and barrier disruption [15]. In parallel, T-helper 17 (Th17) cells contribute to the inflammatory milieu by secreting IL-17, which sustains colonic inflammation [2,14].

Alongside immune dysregulation, the gut microbiome in UC is markedly altered, characterized by a reduction in butyrate-producing commensals that are critical for epithelial homeostasis. These microbial shifts enhance immune activation via pattern recognition receptors (PRRs), thereby perpetuating chronic inflammation. The persistent inflammatory microenvironment also induces oxidative stress, as reactive oxygen species (ROS) generated by activated immune cells inflict further epithelial damage, creating a self-reinforcing cycle of inflammation, oxidative injury, and mucosal dysfunction [11,16].

Signalling Pathways

Pro-inflammatory cytokines TNF-α and IL-1β trigger NF-κB transcription factor, which again increases the production of chemokines, cytokines, and adhesion molecules that sustain inflammation in UC. Additionally, the IL-13 induced STAT6 signaling cascade plays a critical role, elevated levels of phosphorylated STAT6 are found in colonic epithelium of UC patients, and its inhibition reverses IL-13–mediated epithelial damage. The pathophysiology of Ulcerative Colitis as shown Figure 1 below [16,17].

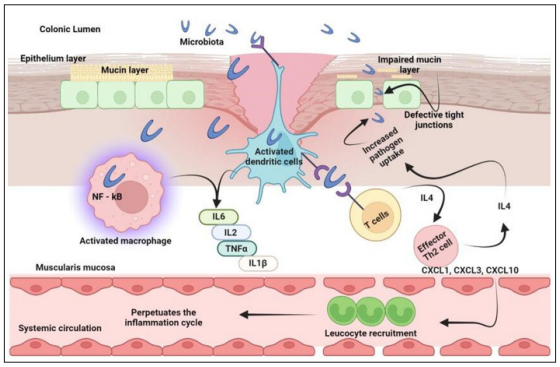

Figure 1: Pathophysiology of Ulcerative Colitis [17]

African Medicinal Plants Used Traditionally for GI Disorders

Despite their longstanding role in primary healthcare, the contributions of traditional healers and medicinal plants are often underappreciated in formal medical practice across Africa. Nonetheless, many families rely on locally available and affordable herbal remedies for common gastrointestinal (GI) ailments such as diarrhea, dysentery, abdominal pain, and peptic ulcers. Ethnobotanical surveys from diverse regions including Nigeria, Niger, and South Africa consistently document a rich repository of indigenous knowledge regarding the use of specific plant species and plant parts. Leaves, bark, and roots are most frequently utilized, typically prepared as decoctions, infusions, or macerations for oral administration Table-1 summarizes commonly African Plants Used Traditionally for GI Disorders [18,19].

Phytochemical analyses of these species often reveal the presence of flavonoids, tannins, terpenoids, saponins, and alkaloids-bioactive classes of compounds associated with antimicrobial, antioxidant, anti-secretory, and mucosal-protective properties. Laboratory and preclinical studies lend further support to these traditional claims. For instance, Euphorbia hirta extracts demonstrate gastroprotective activity in rodent ulcer models, Vernonia amygdalina extracts mitigate castor oil–induced diarrhea in mice, and Aloe vera gel reduces colonic damage in experimental models of ulcerative colitis [20-23]. Collectively, these findings highlight the therapeutic potential of African medicinal plants and underscore the need for further pharmacological and clinical validation.

Table 1: African Plants Used Traditionally for GI Disorders

S/N	African plants (Scientific Name)	Traditional GI Use
1	Euphorbia hirta L.	Used in diarrhea and ulcers; gastroprotected in animal models [21].
2	Psidium guajava L. (Guava)	Antidiarrheal, it inhibits enteric colonization and symptoms [5] [24].

3	Carica papaya L. (Papaya)	Treats diarrhea and gastrointestinal disturbances; anti-inflammatory [25].
4	Vernonia amygdalina Del. (Bitter Leaf)	Used in diarrhea and abdominal discomfort; suppresses castor-oil-induced diarrhea [22].
5	Azadirachta indica A. Juss. (Neem).	Traditional antiseptic/ antidiarrheal and was found to possess gastroprotective and antimicrobial activities in other studies/Ethanolic extract suppressed pro-inflammatory cytokines in TNBS-induced colitis [26].
6	Ocimum gratissimum L. (Scent leaf/African basil)	Used for stomach upsets and diarrhea; contains antioxidants/ anti-inflammatory phytochemicals supportive of GI protection [27].
7	Zingiber officinale Roscoe (Ginger).	Used to treat nausea, dyspepsia and stomach protection; has gastroprotective and anti-inflammatory information [28].
8	Allium sativum L. (Garlic)	Used against infectious GI illness and inflammation; possesses antimicrobial and immunomodulatory action associated with GI infections [29].
9	Aloe barbadensis Miller (Aloe Vera).	Historically applied in ulcers and mucosal healing; models of colitis in animals demonstrate reduced colonic inflammation and damage [23].
10	Moringa oleifera Lam. (moringa)	Applied in diarrhea and GI inflammation; flavonoids and other in vitro antidiarrheal/anti-inflammatory alkaloids occur in leaves/seeds [30].
11	Aframomum melegueta K. Schum. (Grains of paradise)	It has gastroprotective and anti-Helicobacter activity [31].
12	Garcinia kola Heckel (Bitter kola).	Used in traditional medicine against diarrhea and stomachache; seeds/extracts exhibit antimicrobial and anti-secretory activities [32].
13	Combretum molle R.Br. ex G. Don	Used against dysentery and diarrhea; extracts exhibit antibacterial and antioxidant activity validating GI use [20].
14	Sclerocarya birrea (A. Rich.) Hochst. (Marula).	Against stomachache and diarrhea; nutritional and antioxidant research validates GI relevance [33].
15	Terminalia avicennioides (Guill. & Perr.)	This is a stem-bark historically utilized to cure diarrhea; controlled animal studies document antidiarrheal and spasmolytic effects [34].
16	Dysphania ambrosioides (syn. Chenopodium ambrosioides).	Anthelmintic and employed in diarrheal disease; reports antibacterial/antioxidant activity of its oils/extracts [35].
17	Tithonia diversifolia (Hemsl.) A. Gray.	Traditional anti-ulcer and anti-inflammatory treatments utilize it; experimental models demonstrate ulcer-protective activity (sesquiterpene lactones implicated) [36].
18	Clerodendrum myricoides R.Br.	Used in East African traditional medicine for diarrhea; in vivo mouse experiments reveal decreased frequency of diarrhea when extracts from leaves are administered [37].
19	Alstonia boonei De Wild.	Stem-bark used as antidiarrheal/ antispasmodic [38].

Bioactive Compounds with Anti-Colitis Properties

Bioactive molecules are chemical substances present naturally in plants which exhibit biological activities in the biological tissue, and bioactive classes of molecules found in medicinal plants including flavonoids, terpenoids, alkaloids, saponins and phenolic acid [18]. By "anti-colitic" effect, we are referring to the capacity of a drug or extract to suppress the inflammation, mucosal damage, ulceration, hemorrhaging or pro-inflammatory signaling in the colon in experimental models or, less commonly, in man [23,28].

Within phytochemical subclasses as showed in Figure 2 below, flavonoids are always involved in anti-colitic activity since they detoxify reactive oxygen species, suppress pro-inflammatory transcription factors and stabilize the gut barrier [18]. Terpenoids and sesquiterpene lactones (e.g., Tithonia spp. and certain ginger alkaloids) have anti-inflammatory and gastroprotective effects in animal models of colitis, often through down-regulation of pro-inflammatory mediators and mucosal integrity maintenance. Alkaloids and saponins are also found in several African GI remedies and can perform antimicrobial action against enteric pathogens while also modulating host immune responses that trigger inflammation in the colon [18,20,28,36].

Lastly, later extracts, like Aloe vera gel, Moringa oleifera leaf extracts, and Garcinia kola kolaviron, have blended classes of bioactives that work synergistically (antioxidant + anti-inflammatory + mucoprotective), and the synergistic activities are exactly what experimental colitis literature has found to be therapeutic [23,30,32].

Specific Bioactive Compounds and Their Mechanisms

- **Thymoquinone**

This compound is found in black cumin and was observed to have anti-inflammatory activity against colitis through PPAR-γ activation, which is a colonic epithelial transcription factor [39].

- **Curcumin**

A molecule of polyphenol in turmeric, curcumin is antioxidant and anti-inflammatory in nature, which may provide relief from symptoms of ulcerative colitis [5].

- **Quercetin**

This flavonoid, common to most fruits and vegetables, showed a positive anti-IBD effect via remodeling of microbiota of the gut, induction of secretion of mucin, fortifying of the intestinal barrier, and balance of immune regulation as shown in Figure 3 below. [40].

- **Resveratrol**

A polyphenolic molecule present in grapevines and other vegetables, possibly working with anti-inflammatory and antioxidant functions [41].

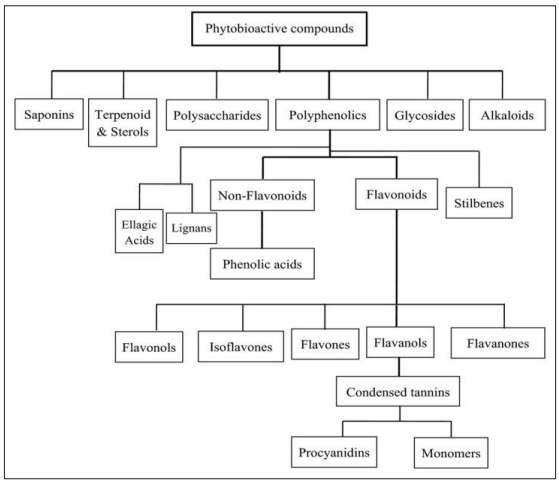

Figure 2: Classification of Phytobioactive Compounds [42].

Pharmacological Mechanism of The Bioactive Compounds

- **Suppression of NF-κB Signaling**

A primary route by which plant bioactives reduce colonic inflammation is suppression of nuclear factor-κB (NF-κB) signaling, which lowers transcription of cytokines such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) that drive mucosal damage; multiple plant extracts including ginger and neem have been shown to suppress NF-κB or downstream cytokines in experimental models [26,28].

- **Down-regulation of COX-2 Expression**

This is followed by modulation of cyclooxygenase-2 (COX-2) and prostaglandin cascades, in which various flavonoid-rich extracts inhibit COX-2 expression and prostaglandin-mediated gut lining edema and ulceration with resulting decreased pain and mucosal injury [18,20].

- **Antioxidant Activity**

Antioxidant activity is another mechanism underlying wherein different bioactives scavenge reactive oxygen and nitrogen species in colon tissue upon inflammation, activate endogenous antioxidant enzymes and thus restrict oxidative damage to epithelial cells. This is a mechanism well established for kolaviron, moringa extracts and flavonoid preparations [18,30,32].

- **Immunomodulation**

The changes towards decreased pro-inflammatory Th1/Th17 responses and enhanced regulatory cytokine profiles, decreased neutrophil migration, and decreased myeloperoxidase activity, has been proved for several extracts in Dextran Sodium Sulfate (DSS) or 2,4,6-Trinitrobenzene Sulfonic Acid (TNBS) models of colitis and is behind the histological improvement with Aloe vera, Psidium guajava and other extracts [5,23,24].

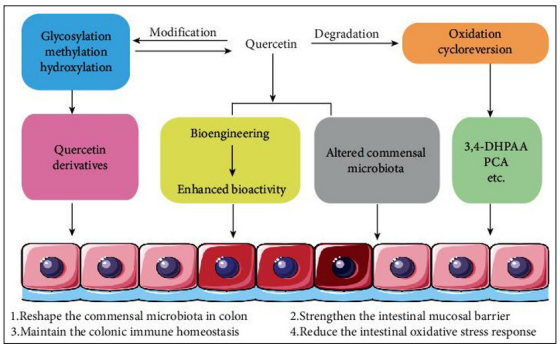

Figure 3: Mechanism of Action of Quercetin [40].

Challenges and Prospects

The path from ethnopharmacologic application of African medicinal plants to ulcerative colitis treatment based on science is impeded by some important bottlenecks. Foremost of these is the absence of standardization in plant procurement, preparation, and dosing, rendering reproducibility challenging. Clinical evidence is still lacking, with most data limited to the laboratory or animal experiments, and safety information, especially regarding long-term use and herb–drug interactions, are not available. Regulatory processes are not always appropriate to the intricate nature of herbal preparations, which delays their approval for clinical use.

In spite of such challenges, hope exists. Analytical chemistry has evolved to the extent that it is able to provide strict characterization of active ingredients, and contemporary clinical trial design is able to provide significant data from small targeted trials. Adding to greater interest in microbiome science and integrative medicine, these trends provide a special window of opportunity to integrate traditional knowledge and science, provided that ethical benefit-sharing and conservation of biodiversity are at the center of development.

Conclusion

Ulcerative Colitis therapy can be complemented or even replaced with African medicinal plants. This is because they contain an untapped pool of bioactive molecules. They have an ethnopharmacological rationale of value and available scientific evidence verifying their anti-inflammatory, antioxidant, and immunomodulatory activities. Actual breakthrough will rely on bridging the divide between old traditions and fixed biomedical evidence, promising species standardized, examined for safety, and analyzed by properly designed clinical trials. If handled judiciously, this crossover between heritage and innovation will produce affordable, culturally appropriate, and scientifically valid therapies to help the patient and the people who kept these medicines alive for centuries.

Recommendation

Future research should prioritize systematic evaluation of African medicinal plants with demonstrated ethnopharmacological use in gastrointestinal disorders. This includes isolation and characterization of bioactive compounds, elucidation of

molecular mechanisms, and rigorous safety assessments. Well-designed preclinical and clinical trials are essential to validate efficacy, standardize dosage, and ensure reproducibility. Collaborative efforts between ethnobotanists, pharmacologists, and clinicians are strongly recommended to integrate traditional knowledge with modern biomedical frameworks. Such an approach will foster the development of affordable, accessible, and culturally relevant therapeutic alternatives for ulcerative colitis.

Consent for Publication

We confirm that all individuals named in the Acknowledgments and Methods sections have agreed to the inclusion of their names and institutional affiliations in this manuscript

Data Availability

All data supporting the findings of this study are available from the corresponding author upon request. The authors affirm that the data have been stored securely and can be accessed for verification or further research in line with institutional and ethical guidelines.

Competing Interests

The authors declare that they have no competing interests

Authors' Contributions

Conceptualization and Design

Blessing Oluwagbamila Omolaso. Data Curation: Blessing Oluwagbamila Omolaso. Methodology: Emmanuel Orire Ikuomola and Deborah Doyin Alade. Resources: Adedoyin Bisola Arogundade. Writing - Original Draft: Blessing Oluwagbamila Omolaso. Review & Editing: Emmanuel Orire Ikuomola, Adedoyin Bisola Arogundade and Deborah Doyin Alade. Final Editing: Emmanuel Orire Ikuomola

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