

Rec. Nat. Prod. X:X (2025) XX-XX

records of natural products

# Botanical, Phytochemistry, Pharmacology and Applications of Genus *Aframomum*: A Review

Yezi Ma 🗅<sup>#</sup>, Haonan Xu 🔎<sup>#</sup>, Yu Sun 🕩, Hao Fan 🔍, Yuze Li, 🔍,

Xiaomei Song 🔍, Wei Wang<sup>\*</sup> 🔍 and Dongdong Zhang 🔘<sup>†</sup>

School of Pharmacy, Shaanxi Key Laboratory of Research and Application of "Taibai Qi Yao", Shaanxi University of Chinese Medicine, Xianyang 712046, China

(Received February 10, 2025; Revised March 17, 2025; Accepted March 18, 2025)

**Abstract**: *Aframomum* belongs to the ginger family Zingiberaceae, a group of perennial herbaceous plants found mainly in tropical Africa, including many countries in West, Central and East Africa. *Aframomum* spp has a long history of medicinal use in African traditional medicine. It has been used to treat a variety of ailments such as digestive disorders (for relief of indigestion, stomach pains, etc.), respiratory disorders (to alleviate symptoms of coughs and colds), and inflammatory diseases. However, there is a lack of current literature summarizing this area. Therefore, the present review aims to comprehensively organize the botanical, phytochemical, and pharmacological studies of *Aframomum* spp to provide reference studies for further discovery of its therapeutic value. For this purpose, relevant information on *Aframomum* spp was searched from scientific databases including Science Direct, Web of Science, Google Scholar, PubMed. Modern studies have shown that *Aframomum* spp contains a variety of chemical constituents containing terpenoids, diarylheptanoids, flavonoids, and lignans, which have various pharmacological effects such as antioxidant, antibacterial, anti-inflammatory and analgesic. The phytoconstituents and various pharmacological activities of *Aframomum* spp. reported in this paper can provide valuable references for further studies.

**Keywords:** *Aframomum*; botanical; phytochemistry; pharmacology; applications. © 2025 ACG Publications. All rights reserved.

The article was published by ACG Publications <u>http://www.acgpubs.org/journal/records-of-natural-products</u> Month-Month 202x EISSN:1307-6167 DOI: <u>http://doi.org/10.25135/rnp.508.2502.3429</u> Available online: April 07, 2025

<sup>\*</sup>Corresponding authors: E-Mail: <u>270468361@qq.com</u> (W. Wang) <u>zhangnatprod@163.com</u> (D. Zhang) #These authors contributed equally to this work

# 1. Introduction

*Aframomum* spp. are widely distributed in Africa and elsewhere as a plant of the Zingiberaceae family. They have long been important in local traditional medicine as remedies for various diseases.

With the continuous development of scientific research methods and techniques, significant progress has been made in exploring the chemical properties of *Aframomum* plants. Among them, terpenoids, diarylheptanoids, vanilloid, and flavonoids have emerged as key constituents, each with unique structural features and chemical properties. Along with chemical studies, their pharmacological effects have also received attention. In vitro and in vivo studies have demonstrated their potential in several therapeutic areas. The compounds extracted and purified from these plants possess significant antioxidant activity, which reduces the production of harmful free radicals and modulates the expression and activity of endogenous cellular antioxidant enzymes, thereby exerting their efficacy. Its antimicrobial capacity has also been demonstrated against a wide range of pathogenic bacteria, promising the development of new antimicrobial agents. In addition, its anti-diabetic and anti-inflammatory effects have been further demonstrated, and it has shown potential in pain relief and even in the prevention and treatment of cancer, but further in-depth research is needed.

In modern life, antioxidant-rich *Aframomum* spp. offer valuable applications for human health, with favorable results in skin protection and obesity prevention. In the field of dietary supplements, extracts or powders of *Aframomum* spp. can be incorporated into functional foods and beverages, and can also be used as natural preservatives for food storage.

The aim of this review is to comprehensively summarize the progress of research on the chemical composition, pharmacological effects and modern applications of *Aframomum* plants in recent years, and to reveal their potential as a valuable source for future drug discovery and development applications.

#### 2. Search methodology

In this paper, a comprehensive study and analysis of previously published literature was carried out to investigate the botanical, phytochemistry, pharmacology, applications of the genus *Aframomum*. All literature on the genus *Aframomum* was collected by using databases such as Medline PubMed, Science Direct, Web of Science, Baidu Scholar, Google Scholar and CNKI. The keywords searched included: *Aframomum*, *Aframomum* citratum, chemical composition of *Aframomum*, applications of the genus *Aframomum*. Some of the analysed studies were obtained by manually searching articles in the reference lists of the included studies. Chemical structures were drawn with Chem Draw Professional 20.0 software. The figures of the pharmacology section and application section were created using Fig draw and WPS.

#### 3. Botanical

Zingiberaceae plants are a family of terrestrial rhizomatous plants with more than 1,400 species distributed in more than 50 genera. *Aframomum* is one of the largest genera of Zingiberaceae plants. renowned for its diverse and often medicinally valuable members. These plants are typically characterized by their lush, perennial growth habit, with large, lanceolate leaves that exhibit a glossy green texture, providing an aesthetically pleasing appearance in their native habitats. *Aframomum* plants range from Senegal in West Africa to Ethiopia in North Africa and south to Angola and Madagascar (distribution shows in Figure 1). It is also found in the islands of the Gulf of Guinea, Sao Tome and Principe. However, some species are ecologically specialized, for example, *A. longilgulatum* is known only from the forests of Cameroon, while the flooded forests of the Congo River basin are dominated by *A. pseudostipu. Aframomum* species also grow in light gaps and forest edges, and are common along roadsides and in old fields. When any part of the plant is crushed it produces an aroma. We searched worldfloraonline.org and found that there are more than 80 species in the genus *Aframomum* and the diversity of the genus *Aframomum* is concentrated in central Africa [1-3].

The inflorescences of *Aframomum* spp. are also a notable botanical feature. They usually bear showy, tubular flowers that come in a variety of colors, ranging from vibrant yellows to warm oranges and even soft pinks, attracting pollinators essential for their reproduction. The flowers are arranged in dense spikes or racemes, further enhancing their visual impact. From a taxonomic point of view, the genus is challenged by its variable morphology and relies on a combination of traditional morphological characters and modern molecular techniques to accurately classify and distinguish the many species in the genus *Aframomum*. This has led to a more refined understanding of their phylogenetic relationships, which in turn has implications for tracing the evolution of their chemical constituents and pharmacological properties. In terms of ecological adaptation, *Aframomum* spp. has shown remarkable versatility. They can be found in a range of habitats, from humid rainforests to more arid savannah regions, adjusting their growth patterns and physiological processes accordingly [4-6].

A. melegueta is gradually becoming extinct and scholars used a completely randomized design with three replications to set up test plots and examined the use of cocoa, oil palm and fallow land. The results showed that the main challenge in growing A. melegueta is the lack of external market (33.3%) and most farmers preferred fallow land (73.9%) to grow A. meleguta. growing A. melegueta in tree farms in non-reserve areas can help to increase production and thus improve the livelihood of farmers. Farmers are encouraged to plant this species in cocoa farms, oil palm farms and fallow lands [7]. In addition, it has been found that a viable system for efficient conservation and genetic improvement of A. melegueta can be provided by increasing the efficiency of genetic transformation [8]. The recent collection of a large number of A. melegueta genotypes from major growing areas in Ethiopia by the Jimma Agricultural Research Institute to analyze genetic variation among genotypes and to produce varieties suggests that varieties, environmental and soil factors, and management practices may have an impact on these variations [9]. It has also been shown that the morphological characteristics of A. melegueta are greatly influenced by its ecological habitat [10].

*A. corrorima* is one of the most endangered indigenous spice and medicinal plant species in Ethiopia. Scholars assessed the characterization of its genetic diversity. The results showed that the

degree of genetic diversity of *A. corrorima* populations in southern and southwestern Ethiopia appeared to be high. West Omo, Sheka, Gofa and Basseto populations showed the highest genetic diversity. Therefore, these areas can be used as key sites for *A. corrorima* conservation strategies [11]. In addition, another study showed that *A. corrorima* in general, and collections in particular, in Ethiopia have potential for further improvement and commercialization [12].

Overall, species loss is now at an unprecedented level due to anthropogenic habitat destruction and climate change, and new technologies are urgently needed today to protect these rapidly disappearing species. The currently accepted name and synonyms of the plant were verified on "World Flora Online" (www.worldfloraonline.org).

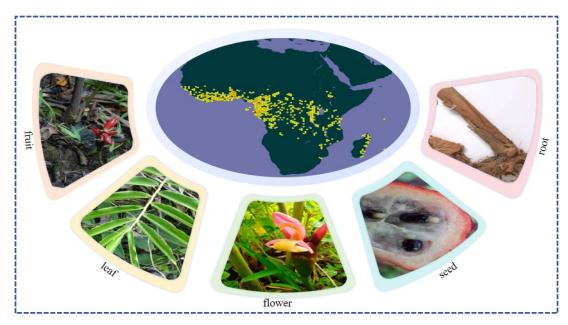


Figure 1. Distribution of Aframomum in Africa

### 4. Phytochemistry

#### 4.1. Diarylheptanoids and Vanilloid

Diarylheptanoids typically possess a characteristic chemical structure, consisting of two aromatic rings connected by a seven-carbon chain. This structural motif endows them with particular physical and chemical properties. They are often involved in various biological activities. In plants, they can play roles in defense mechanisms against pathogens and pests. Vanilloid compounds, on the other hand, are renowned for their pungent and characteristic odor, similar to that of vanilla. Structurally, they usually contain a vanillyl group, which is responsible for their distinct flavor and aroma. In nature, vanilloid compounds are found in these plants and are involved in multiple physiological processes, antioxidant and antimicrobial effects are included. The names and structures of these two classes are shown in Table 1 and Figure 2.

Ma et.al., Rec. Nat. Prod.	(20XX)	X:X XX-XX
----------------------------	--------	-----------

No.	Compound	Plant	Parts	Ref.
1	6-gingerol	A. meleguea	seeds, fruit	[13-15]
2	6-paradol	A. meleguea	seeds, fruit	[13-15]
3	8-dehydrogingerdione	A. meleguea	seeds	[13]
4	8-gingerol	A. meleguea	seeds	[13, 14]
5	dihydro-6-paradol	A. meleguea	seeds	[13]
6	4-[2-(5-butylfuran-2-yl)-ethyl]-2- methoxyphenol	A. melegueta	seeds	[16]
7	methyl-6-gingero	A. melegueta	seeds	[16]
8	6-gingerdione	A. melegueta	seeds	[16]
9	rac-6-dihydroparadol	A. melegueta	seeds	[16]
10	6-gingerdiols 3 <i>S</i> ,5 <i>S</i> -1-(4-hydroxy-3- methoxyphenyl)-decane-3,5-diol	A. melegueta	seeds	[16]
11	3 <i>R</i> ,5 <i>S</i> -1-(4-hydroxy-3-methoxyphenyl)-decane- 3,5-diol	A. melegueta	seeds	[16]
12	6-shogaol	A. melegueta	seeds, fruit	[14, 15, 17]
13	(S)-9-hydroxy-6-paradol	A. melegueta	seeds	[17]
14	(9S)-3,9-dihydroxydihydro-6-paradol	A. melegueta	seeds	[17]
15	(3 <i>S</i> ,5 <i>S</i> )-3,5-dihydroxy-1-(4-hydroxy3- methoxyphenyl)-decane	A. melegueta	seeds	[17]
16	4-gingerdiol	A. melegueta	seeds	[17]
17	dehydro-6-gingerdione	A. melegueta	seeds	[17]
18	6-dehydroparadol	A. melegueta	seeds	[18]
19	paradol	A. letestuianum	seeds	[19]
20	4-shogaol	A. letestuianum	seeds	[19]
21	7-paradol	A. melegueta	seeds	[20]
22	1-(4'-hydroxy-3'-methoxyphenyl)-decan-3-ol	A. melegueta	seeds	[20]
23	acetyl-6-gingerol	A. melegueta	seeds	[20]
24	1-(4'-hydroxy-3'-methoxyphenyl)-5-methoxy- dodecan-3-one	A. melegueta	seeds	[20]
25	1-dehydrogingerdione	A. melegueta	seeds	[20]
26	1-(4'-hydroxy-3'-methoxyphenyl)-5-methoxy- decan-3-one	A. melegueta	seeds	[20]
27	1-(4'-hydroxy-3'-methoxyphenyl)-3-octen-5- one	A. melegueta	seeds	[20]
28	1-(4-hydroxy-3-methoxyphenyl) decan-3-one	A. melegueta	seeds	[21]
29	5-oxo-l-(4-hydroxy-3-methoxyphenyl) decan- 3-one	A. melegueta	seeds	[22]
30	1-(4-hydroxy-3-methoxyphenyl) decan-5-en-3- one	A. melegueta	seeds	[22]

**Table 1.** Diarylheptanoids and vanilloid compounds from Aframonum

Phytochen	nistry and	p	harmacol	logy	of	genus A	1 <i>framomum</i>

		5 of genus fijt an	iomum	
31	5-hydroxy-l-(4-hydroxy-3-methoxyphenyl) decan-3-one	A. melegueta	seeds	[22]
32	1,5-bis-(3,4-methylenedioxyphenyl) pent-1,4- dien-3-one	A. melegueta	seeds	[22]
33	dihydrogingerenone A	A. meleguea	seeds	[13, 14]
34	dihydrogingerenone C	A. meleguea	seeds	[13, 14]
35	1,7-bis(3,4-dihydroxy-5-methoxyphenyl)- heptane-3,5-diyl diacetate	A. meleguea	seeds	[13]
36	3-( <i>S</i> )-acetyl-1-(4',5'-dihydroxy-3'- methoxyphenyl)-7-(3",4"-dihydroxyphenyl)- heptane	A. melegueta	seeds	[14]
37	3,5-diacetoxy-1-(3',4'-dihydroxylphenyl)-7- (3",4"-dihydroxy-5"-methoxyphenyl) heptane	A. melegueta	seeds	[14]
38	1-(4-hydroxy-3-methoxyphenyl)-7-(4- hydroxyphenyl)-3-heptanone	A. melegueta	seeds	[17]
39	(4 <i>E</i> )-1-(4-hydroxy-3-methoxyphenyl)-7-(4- hydroxyphenyl) -(4 <i>E</i> )-4-hepten-3-one	A. melegueta	seeds	[17]
40	letestuianin A	A. letestuianum	seeds	[23]
41	letestuianin B	A. letestuianum	seeds	[13]
42	letestuianin C	A. letestuianum	seeds	[13]
43	gingerenone D	A. letestuianum	seeds	[19]
44	dihydrogingerenone B	A. letestuianum	seeds	[19]

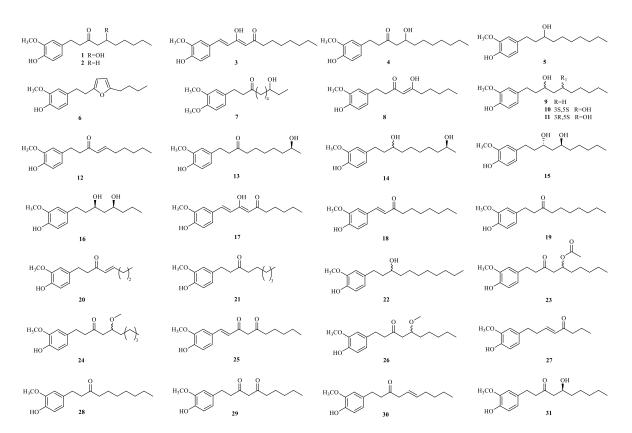


Figure 2. Structure of Diarylheptanoids and vanilloid compounds

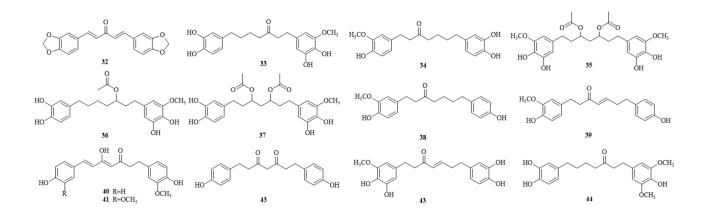


Figure 2. Structure of Diarylheptanoids and vanilloid compounds (continued..)

## 4.2. Terpenoids

*Aframomum* contains a wide variety of terpenoids, mainly diterpenes, as well as sesquiterpenes and triterpenes. Diterpenoids, with 20-carbon frameworks, are typically more complex in structure. In *Aframomum* spp., they have been found to possess potential pharmacological activities. Some diterpenoids exhibit antioxidant properties, capable of scavenging free radicals and safeguarding the plant's cells from oxidative stress. Their names and structures are shown in Table 2 and Figure 3.

No.	Compound	Plant	Parts	Ref.
45	aulacocarpinolide	A. aulacocarpos	seeds	[24]
46	( <i>E</i> )-labda-8(17),12-diene-15,16-dial	A. daniellii	seeds, rhizomes	[25]
47	( <i>E</i> )-8 $\beta$ ,17-epoxy-labd-12-ene-15,16-dial	A. daniellii, A. sceptrum	seeds, rhizomes, fruits	[26, 27]
48	aulacocarpin A	A. zambesiacum	seeds	[28]
49	aulacocarpin B	A. zambesiacum	seeds	[28]
50	3-deoxyaulacocarpin A	A. zambesiacum	seeds	[28]
51	methyl-14ζ,15-epoxy-3β-hydroxy- 8(17),12E-labdadien-16-oate	A. zambesiacum	seeds	[28]
52	$8\beta$ ,17-epoxy-12 <i>E</i> -labdene-14 $\xi$ ,15,16-triol	A. zambesiacum	seeds	[28]
53	galanolactone	A. zambesiacum	seeds	[28]
54	zambesiacolactone A	A. zambesiacum	seeds	[28]
55	zambesiacolactone B	A. zambesiacum	seeds	[28]
56	(E)-8(17),12-labddiene-15,16-dial	A. latifolium, A. sceptrum	fruits, leaves	[27]

Table 2. Terpenoids from the genus Aframomum

	Phytochemistry and pharma	acology of genus Af	ramomum	
57	(E)-15,15-diethoxylabda-8(17),12-dien-	A. latifolium, A.	fruits, leaves	[27]
57	16-al	sceptrum	ffuits, leaves	[27]
50	oonononin D	A. latifolium, A.	funite leaves	[27]
58	coronarin B	sceptrum	fruits, leaves	[27]
50	1 1 4	A. latifolium, A.	6 . 1	[07]
59	galanal A	sceptrum	fruits, leaves	[27]
<b>C</b> 0	1 10	A. latifolium, A.	6 1	[07]
60	galanal B	sceptrum	fruits, leaves	[27]
61	aframolin A	A. longifolius	seeds	[29]
62	aframolin B	A. longifolius	seeds	[29]
63	labda-8(17),12(E)-diene-15,16-dial	A. longifolius	seeds	[29]
64	aulacoarpinolide	A. aulacocarpos	seeds	[30]
65	8α-isomer	A. aulacocarpos	seeds	[31]
	methyl 14ξ,15-epoxy 8(17),12E-	A		[21]
66	labdadiene-16-oate	A. aulacocarpos	seeds	[31]
67	(E)-14-hydroxy-15-norlabda-8(17),12-	A	<b>40.04</b> 0	[20]
67	dien-16-al	A. melegueta	roots	[32]
68	16-oxo-8(17),12( <i>E</i> )-labdadien-15-oic acid	A. melegueta	roots	[32]
60	$8\beta$ ,17-Epoxy-11,15-epoxy-15-hydroxy-	A mile at m	aaada	[22]
69	12-labden-16-al	A. sulcatum	seeds	[33]
70	8β,17-epoxy-11,15-epoxy-15-acetoxy-12-	A and a struct	aaada	[22]
70	labden-16-al	A. sulcatum	seeds	[33]
71	sulcanal	A. sulcatum	seeds	[33]
72	sceptrumLabdalactone A	A. sceptrum	rhizomes	[34]
73	sceptrumLabdalactone B	A. sceptrum	rhizomes	[34]
74	$8\beta$ ,17-epoxy- $3\beta$ , $7\beta$ -dihydroxy- $12(E)$ -	1 saantuum	seeds	[25]
/4	labden-16,15-olide	A. sceptrum	seeus	[35]
75	methyl8 $\beta$ ,17-epoxy-3 $\beta$ ,7 $\beta$ ,15-	A scontrum	seeds	[35]
15	trihydroxy12(E)-labden-16-oate	A. sceptrum	seeus	[33]
76	$3\beta$ , $7\beta$ , $8\beta$ , $12\xi$ , $17$ -pentahydroxylabdan-	A. sceptrum	seeds	[35]
70	16,15-olide	A. sceptrum	seeus	[33]
77	aulacocarpin C	A. aulacocarpos	seeds	[36]
78	aulacocarpin D	A. aulacocarpos	seeds	[36]
79	$8\beta(17)$ -epoxy-14,15,16-triacetoxy labd-	A. aulacocarpos	seeds	[36]
19	12( <i>E</i> )-ene.	A. autacocarpos	seeus	
80	17-hydroxy-14,15,16-triacetoxy labda-	A. aulacocarpos	seeds	[36]
80	8( <i>E</i> ),12( <i>Z</i> )-diene	A. autacocarpos	seeus	
81	17-hydroxy-14,15,16-triacetoxy labda-	A. aulacocarpos	seeds	[36]
01	7( <i>E</i> ),12( <i>Z</i> )-diene	A. unucocurpos	seeus	
82	$15,16$ -epoxy- $12\beta$ -methoxylabda- $8(17)$ -	1 gulgaoagmos	saads	[36]
02	13(16),14-triene	A. aulacocarpos	seeds	
83	6,7-epoxy-3(15)-caryophyllene	A. arundinaceum	seeds	[37]
84	(–)-α-bisabolol	A. arundinaceum	seeds	[37]

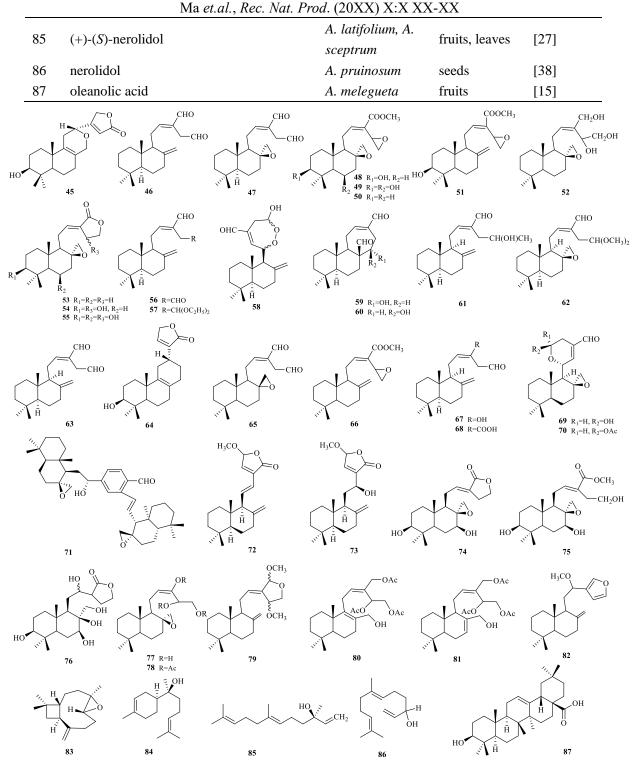


Figure 3. Terpenoids from the genus Aframomum

# 4.3. Flavonoids and Other Compounds

Flavonoids have a typical  $C_6$ - $C_3$ - $C_6$  basic backbone structure, which gives them diverse chemical properties. The number and position of phenolic hydroxyl groups and the substituents on the rings in their molecular structure are different, resulting in their different pharmacological effects. Moreover, lignans and sterols have been found in *Aframomum*. Their names and structures are shown in Table 3 and Figure 4.

No.	Compound	Plant	Parts	Ref.
88	kaempferol 3,7,4'-trimethyl ether	A. giganteum	stems	[39]
89	quercetin 3,7,3',4'-tetramethyl ether	A. giganteum	stems	[39]
90	quercetin 3,7,4'-trimethyl ether	A. giganteum	stems	[39]
91	5-hydroxy-7-methoxy flavone	A. melegueta	roots	[32]
92	apigenin	A. melegueta	roots	[32]
93	kaempferol	A. melegueta	seeds	[40]
94	naringenin	A. melegueta	seeds	[40]
95	rutin	A. melegueta	seeds	[40]
96	catechinn	A. melegueta	seeds	[40]
97	epicatechin	A. melegueta	seeds	[40]
98	2 <i>R</i> ,3 <i>R</i> -(+)-3-acetoxy-4',5-dihydroxy-7- methoxy flavanone	A. pruinosum	seeds	[38]
99	2 <i>R</i> ,3 <i>R</i> -(+)-3-acetoxy-4',5,7-trihydroxy-flavanone	A. pruinosum	seeds	[38]
100	4',7-di-O-methyl-aromadendrin	A. pruinosum	seeds	[38]
101	7-O-methyl-aromadendrin	A. pruinosum	seeds	[38]
102	3-acetoxy-4',5,7-tri-O-methyl-aromadendrin	A. pruinosum	seeds	[38]
103	3,4',7-triacetoxy-aromadendrin	A. pruinosum	seeds	[38]
104	spartein	A. melegueta	seeds	[40]
105	flavan-3-ol	A. melegueta	seeds	[40]
106	resveratol	A. melegueta	seeds	[40]
107	$\beta$ -sitosterol	A. melegueta	seeds	[40]
108	(–)-buplerol	A. melegueta	roots	[32]
109	(-)-arctigenin	A. melegueta	roots	[32]
110	enterolactone	A. letestuianum	seeds	[19]
111	enterodiol	A. letestuianum	seeds	[19]

Table 3. Flavonoids and other compounds from the genus Aframomum

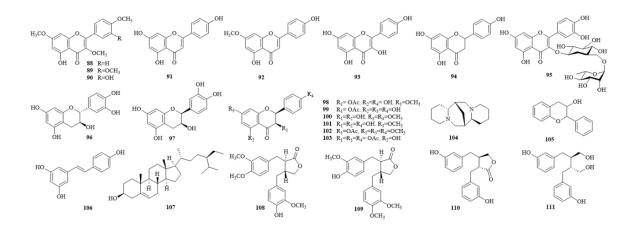


Figure 4. Flavonoids and other compounds from the genus Aframomum

# 5. Pharmacological Effects

#### 5.1. Antioxidant Effect

Scholars analyzed the antioxidant capacity of edible spices in Southern Nigeria and found that Aframomum citratum had the highest amount of total phenol, flavonoid and 1,1-diphenyl-2-picrylhydrazyl radical (DPPH) scavenging ability. Indicating a good nutritional profile and antioxidant potential [41]. It was shown that the therapeutic capacity of T. tetraptera and A. citratum used as spices is attributed to their bioactive molecules including polyphenols. Experiments using phenolic extracts of these two spices to study their antioxidant potential showed significant (p < 0.05) dosedependent free radical scavenging activity and significant inhibition of bovine serum albumin and 5-Lipoxygenase (5-LOX) denaturation [42]. Species of the genus Aframomum are widely used in folk medicine as dietary supplements and medicines for the treatment of a wide range of diseases. Stephen et al. investigated the acetylcholinesterase inhibitory activity and antioxidant properties of phenolicrich extracts of A. danielli and A. melegueta. The acetylcholinesterase inhibitory activity and antioxidant properties were assessed by in vitro modeling to inhibit quinolinic acid [17], 2, 2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and DPPH radical scavenging ability. The results showed that both extracts exhibited dose-dependent acetylcholinesterase inhibitory activity (125-1000  $\mu$ g/mL), whereas the acetylcholinesterase inhibitory activity of A. danielli extract (IC<sub>50</sub>=373.33  $\mu$ g/mL) was significantly higher than that of A. melegueta extract (IC<sub>50</sub>=417.10  $\mu$ g/mL). In addition, both extracts significantly reduced QA-elevated Malondialdehyde (MDA) content, reduced Fe<sup>3+</sup> to Fe<sup>2+</sup>, and scavenged DPPH and ABTS radicals (p < 0.05) [31].

Phytochemical composition and antioxidant activity of methanolic extracts of five spices from Cameroon were analyzed by scholars. The extracts with the highest total phenolic and flavonoid contents were found to exhibit the strongest antioxidant activity, as determined using DPPH and ABTS free radical scavengers. The results indicated that the analyzed extracts, especially Xyopia aethiopica and Aframomum citratum are potential sources of natural antioxidants [43]. The study evaluated the antioxidant effect of methanolic seed extracts of A. melegueta. The antioxidant effect was assessed in vitro, by DDPH photometric and reactant assay like Superoxide dismutase (SOD), Catalase (CAT). The extracts (concentrations of 25-400 µg/mL) produced a concentration-dependent increase in antioxidant activity in the DDPH method. The extracts (400  $\mu$ g/mL) showed a significant increase in SOD and CAT activities and a significant decrease in the level of TBARS reactive substances compared to the control. It suggests that the seeds of A. melegueta have potent antioxidant activity or can be used as an antioxidant supplement (p < 0.05) [44]. In addition, the researchers prepared non-alcoholic beverages containing palm sugar and A. melegueta as raw materials and tested their physicochemical, nutritional, and antioxidant properties to determine their suitability as a functional refreshing beverage with good nutritional value. The results showed that A. melegueta DDPH free radical scavenging activity and reducing power levels were low  $(12.40 \pm 0.20)$ . Moreover, a study by Gabriel et al. confirmed the strong antioxidant capacity of A. melegueta [45, 46]. Another study evaluated the in vitro and in vivo antioxidant and cytotoxic potential of ethanol and methanol extracts of A. melegueta and analyzed their chemical profiles. High Performance Liquid Chromatography (HPLC) analysis identified the key compounds including gallic acid caffeic acid, caffeine, ferulic acid and quercetin, among others. The extracts showed antioxidant activity in DPPH,

FRP assays, indicating their effectiveness as anti-free radical agents. In vivo antioxidant results showed reduced lipid peroxidation levels in serum and liver, highlighting the ability of the extracts to mitigate oxidative stress. In addition, the extracts provided protection against  $H_2O_2$ -permeable erythrocyte hemolysis and modulated NO production in peritoneal macrophages. These findings suggest the potential of *A. melegueta* extracts in strategies for coping with oxidative stress-associated chronic diseases [47]. The study investigated the effects of seed extracts of *A. melegueta* on leukocyte migration and red blood cells (RBCs) in phenylhydrazine-treated rats. Its seed extract exhibited potent antioxidant activity and reduced the level of MDA formation in phenylhydrazine-treated rat RBCs [48].

The preservative properties of fragrances from A. citratum, A. danielli, P. capense and M. myristica are well known. Sylvie et al. investigated the potential of these essential oils to be used as preservatives in cosmetic creams. The evolution of the antioxidant activity of essential oil-based creams used during accelerated aging was studied using the Briggs-Rauscher test and the peroxide index, where the essential oils of A. citratum and P. capense showed low cytotoxicity to the cells tested. A. danielli has low cytotoxicity against the human immortalized keratinocytes (HaCaT) epidermal cell line and no cytotoxicity against the Caco-2 cell line. It is suggested that all four essential oils protect against oxidation in cosmetic creams during accelerated aging [49]. Total polyphenol (TPP) total flavonoid (TFLV) content and antioxidant properties were assessed spectrophotometrically. The results showed that both species, fruits from zone V had the highest TPP, TFLV levels and bioactivity [50]. The study examined the total phenolic content, in-vitro antioxidant activity of A. corrorima seed extracts. The aqueous methanolic extract contained higher total phenolic content and total flavonoid content. The DPPH radical scavenging assay had an EC<sub>50</sub> of  $97 \pm 4 \mu g/mL$ , and the iron-reducing antioxidant capacity assay had an EC<sub>50</sub> of 258  $\pm$  15  $\mu$ g/mL, which was significantly higher than that of petroleum ether extract (p < 0.05) [51]. Scholars analyzed the volatile oils of leaves, stems, seeds, rhizomes and fruits of A. danielli by gas chromatography-mass spectrometry (GC-MS). The free radical scavenging capacity of the volatile oils was determined using DPPH and ferric reducing antioxidant power (FRAP). The results showed higher content of Bterpenes (30.94-47.55%) in leaf stems, rhizomes and fruiting leaves, and higher content of 1,8eucalyptin (53.44%) in seed oil. Among them, the seed oil showed high free radical inhibitory activity in the DPPH assay (IC<sub>50</sub> 45.5  $\mu$ g/mL), and the rhizome oil was the most effective in the FRAP assay, suggesting that A. danielli seed and rhizome oils have the potential as potential botanical resources and are worthy of further bioexploitation [52].

Researchers evaluated the anti-aging effects of a natural mixture of *A. angustifolium* seed extract containing labdane diteroids on normal human keratinocytes or normal human fibroblasts using low-density DNA microarrays. It was found to modulate antioxidant defense, dermal-epidermal junction components and epidermal renewal-related genes. Thus, it has both protective and therapeutic anti-aging effects on the skin [53]. Huguette et al. investigated the chemical composition of the leaves and rhizomes of *A. giganteum* obtained by water vapor distillation by gas chromatography-hydrogen flame ionization detector and gas chromatography-mass spectrometry analysis. The major compounds in the leaf oil were *cis*-pinocamphone (54%) and pinocarvone (10.1%), while the rhizome essential oil consisted mainly of sesquiterpenoids i.e. B-caryophyllene (10.5%) and its oxo derivatives (40%). And the antioxidant and antiradical activities of both samples were evaluated by comparing the antioxidant and antiradical activities of the oils with BHT (Butyl

hydroxytoluene) and the results showed that the IC<sub>50</sub> of the leaf essential oil=1 g/L (IC<sub>50</sub> (BHT)=102  $\mu$ g/L) [54].

Ishola examined the effect of ethanolic seed extract of A. melegueta on scopolamine-induced cognitive impairment in rodents. The results showed that its ethanolic seed extract significantly reduced spontaneous alternating behavior (38.72%) in mice in the Y-maze, in addition to preventing scopolamine-induced spatial learning deficits in the Morris water maze task. Similarly, scopolamineinduced oxidative nitrification stress was attenuated by A. melegueta treatment, as evidenced by a decrease in malondial dehyde (MOD) and nitrite levels and restoration of glutathione (p < 0.05) [55] and SOD levels [56]. A. melegueta seed extracts showed, in a variety of free-radical scavenging, reducing, and chelating assays, as well as in cholinesterase, tyrosinase, and glucosidase assays strong antioxidant and enzyme inhibitory potential. Correlation analysis showed that several specific metabolites of Aspergillus niger were directly correlated with the antioxidant and enzyme inhibitory activities studied [57]. Adigun et al. evaluated the antioxidant and antihyperlipidemic activities in Triton X-100-induced hyperlipidemic rats. The phytochemical composition of the extracts was identified using gas chromatography coupled to mass spectrometry. In vitro antioxidant activity of the extracts (0.2-1.0 mg/mL) was investigated and the results showed that the extracts concentrationdependently scavenged DPPH, H<sub>2</sub>O<sub>2</sub>, and OH<sup>-</sup> radicals. The activities of SOD, glutathione peroxidase (GSH-Px) and glucose-6-phosphate dehydrogenase (G6PD) were reduced, as well as the concentrations of MDA and protein carbonyls, mediated by TritonX-100. The antioxidant and antihyperlipidemic properties of the alcoholic extract of A. melegueta seeds were demonstrated. Additionally, the extracts provided protection against H<sub>2</sub>O<sub>2</sub>-induced erythrocyte hemolysis and modulated NO production in peritoneal macrophages [58, 59].

# 5.2. Antibacterial and Insecticidal Effects

The compounds isolated from the seeds of A. melegueta were experimentally assayed for antimycobacterial activity and minimal inhibit concentration (MIC) against antibiotics by scholars. The results showed that 6-paradol, 8-gingerol and rac-6-dihydroparadol were the most effective inhibitors of ethidium bromide (EtBr) efflux against <sup>M. smegmatis</sup> MC2 155. Their inhibitory activity against EtBr efflux was comparable to that of the reference inhibitor (MIC of EtBr=8 mg/L) [16]. The compound 3-Deoxyaulacocarpin A derived from the seeds of A. zambesiacum showed a strong inhibitory effect on Plasmodium falciparum with an IC<sub>50</sub> value of 4.97  $\mu$ M [28]. The compounds isolated from A. latifolium were tested for in vitro anti-plasmodium falciparum activity and the researchers found that aframodial, coronarin B, and galanolactone showed good inhibitory activity with IC<sub>50</sub> values of 24-56  $\mu$ M [27]. Essential oils of seeds, pericarp, leaves and rhizomes of A. dalzielii, A. letestuianum and A. pruinosum growing in Cameroon were obtained by hydrodistillation and evaluated for antimicrobial activity and found to be the most active against E. coli. The lowest MIC values (0.19-0.39  $\mu$ L/mL) were obtained for the seed essential oils [60]. Researchers assessed the relative toxicity of oily acetone extracts and powder formulations from Piper guineense fruits, Dennettia tripetala seeds, and Aframomum meleguetawith respect to Sitophilus zeamais. Knot where Pguineense was the most toxic followed by D. tripetala and A. melegueta. The order of toxicity of the powder preparations was D. tripetala > A. melegueta > P. gusignificantineense [61]. A. danielli from Zingiberaceae was found to have antibacterial activity against all Gram-positive and Gram-negative bacteria [62]. Compound aframodial showed antimicrobial activity against Cryptococcus neoformans,

Staphylococcus aureus and methicillin-resistant S. aureus (MRS) [29]. Extracts of methanol, nbutanol and chloroform extracts of A. melegueta seeds showed significant anti-adhesion activity against Staphylococcus aureus and lung cancer cell lines. The compound 3-(S)-acetyl-1-(4',5'dihydroxy-3'-methoxy-phenyl)-7-(3'',4''-dihydroxyphenyl) heptane, 6-paradol, 6-shogaol, 8-gingerol, dihydro-6-paradol showed significant anti-adhesion activity, the inhibition of S. aureus adhesion was 60.58%, 50%, 70.07%, 85.4%, 59.85% at 50 mg/mL, respectively (p<0.05) [14].

The study reports the supercritical CO2 extraction of oil from the seeds of Korarima (A. corrorima) and evaluation of its antimicrobial activity. The extracted oil was analyzed by gas chromatography-mass spectrometry (GC-MS) and the major components were nerolidol (33.97-41.20%), geraniol (23.08-24.50%), and  $\alpha$ -terpinene (8.90-9.06%), the oil showed significant antimicrobial activity against Staphylococcus aureus with a minimum inhibitory concentration of 1 mg/mL (p<0.05) [63]. Antibacterial activity of six medicinal plant extracts (water and ethanol) was assessed against Aspergillus singularis (ATCC21784), Pseudomonas aeruginosa (ATCC27856) and Aspergillus fumigatus using agar-well diffusion method. The results showed that liquid and ethanolic extracts of A. melegueta, Moringa oleifera and Cola nitida exhibited consistent inhibitory effects against the target bacteria. The ethanolic extract of A. melegueta showed superior inhibitory activity [64]. The essential oil from the rhizomes of A. sceptrum (Zingiberaceae) was analyzed by GC-MS and found to contain  $\beta$ -pinene (12.7%), caryophyllene oxide (10.0%), and cyperene (6.0%) as the major components. The antimicrobial activity of the oil with β-pinene, caryophyllene oxide and cyperene was also evaluated. The essential oil of A. sceptrum exhibited bacteriostatic activity against Gram-positive bacteria Bacillus subtilis, Staphylococcus epidermidis, and Staphylococcus scepticus. In addition, it exhibited mild bactericidal activity against Candida albicans and Aspergillus fumigatus and significant antiprotozoal activity against Trypanosoma brucei (mLC of 1.51 µl/mL)) and *Trichomonas vaginalis* (IC<sub>50</sub> of 0.12±002 and mLC of 1.72  $\mu$ l/mL; (p<0.05) [65].

Scholars explored the antimicrobial and antiviral capacity of 4-shogaol isolated from A. melegueta seeds against Gram-negative bacteria (Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae and Serratia marcescens). The results showed that the antimicrobial action of 4-shogaol mainly involved disruption of bacterial cell membranes and plasma pumps. It also possesses antipathogenic effects, effectively protecting mice from Pseudomonas aeruginosa infection by reducing biofilm development and inhibiting pathogenic factor production [66]. The antimicrobial activity of three A. chrysanthum seeds extracts against microorganisms was studied using paper diffusion method. The n-hexane and ethyl acetate extracts showed varying degrees of antimicrobial activity against the pathogenic microorganisms studied, especially Staphylococcus aureus. Susceptibility tests carried out on all the extracts showed that n-hexane extract at 200 mg/mL exhibited moderate antibacterial activity against Staphylococcus aureus, Candida albicans and Trichophyton rubrum [67]. Akpan et al. evaluated the inhibitory potential of A. melegueta and Piper guineense extracts against cucumber fruit rot pathogens (strains: Fusarium oxysporium and Penicillium sp). Test plant extracts were prepared at 100% and 70% concentrations. Among them A. melegueta inhibited the growth of Penicillium sp. at 100% concentration with a circle of inhibition of 15.5 mm and 70% concentration of the same plant extracts with a circle of inhibition of 11.5 mm. The aqueous solution of plant extracts showed circle of inhibition of 15.5 mm at 100% concentration and no inhibition at 70% concentration [68]. A. danielli was found to have the potential to inhibit aflatoxins and B1, B2, G1 and G2 aflatoxins.

Combined experimental data showed that the reduction (percentage) of aflatoxin B1 and total aflatoxins after treatment with *A. danielli* were 75.58-8422, 80.54-9746, 25.82-8054, 21.98-659841.08-8307 and 24.84-6165, respectively. aflatoxin-producing molds were also reduced in the treated samples were also reduced in the treated samples. Therefore, treatment of melon seeds with *A. danielli* natural plants prior to storage may reduce the risk of aflatoxin contamination in the post-harvest stage [69]. Another study showed that *A. idanielli* also inhibited Listeria monocytogenes LCDC 81861 with a minimum inhibitory concentration (MIC) of 390 ppm [70].

A study evaluated the effectiveness of A. melegueta in protecting stored Zea mays L. from Sitophiluszeamais Motschulsky. In the test, treated cobs showed significantly higher seed germination compared to untreated cobs, and the use of this repellent material for grain protection has important practical applications. In addition, the use of repellents to protect stored maize grains has the potential to minimize the need for broad-spectrum toxic insecticides, thereby reducing insecticide development (p < 0.05) [71]. In a four-way olfactometer bioassay, alligator pepper, A. melegueta and Z. officinale were studied for Sitophilus zeamais (Coleoptera: Curculionidae) Repellent activity. The results showed that vacuum distilled extracts of A. melegueta and Z. officinale were repellent to adult S. zeamais in the presence and absence of maize (Zea mays) grains. Suggesting their potential in the conservation of stored products at the small-scale farmer level in Africa [72]. A study was conducted to investigate the potential of A. melegueta leaf and seed as a biopesticide against Sitotroga cerealella. The dosage of leaf and seed powder of A. melegueta was 0.1 g, 0.2 g, 0.4 g, 0.6 g, 0.8 g, and the dosage of extract was 1%, 2%, 3%, 4% and 5%, respectively. Insect mortality was recorded on both rice varieties 24, 48 and 72 hours after application of powder and extracts of the plant and the highest number of insects was recorded on FARO52 treated with powder and extracts. And only the seed extract was able to achieve 100% mortality of Sitotroga cerealella at 72 hours after application, indicating that the powder and extract of the plant significantly reduced or prevented the emergence of adult moths (p < 0.05) [73]. The researchers evaluated the effect of essential oils of six plants (Azadirachta indica, A. melegueta, A. daniellii, Clausena anisata, Dichrostachys cinerea, and *Echinops giganteus*) essential oils for their activity against *Trypanosma brucei* TC221. The results showed that A. danielli and E. giganteus were the most active with half-maximum inhibitory concentrations IC<sub>50</sub> of 7.65 and 10.50 µg/mL, respectively [74]. Summarize 5.1-5.2 section in Figure 5.

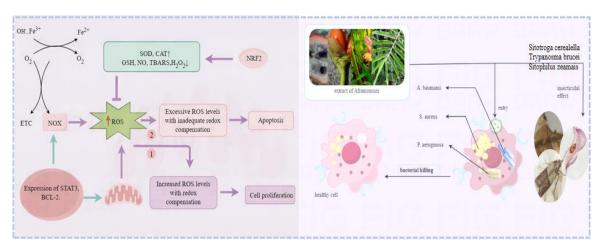


Figure 5. Antioxidant and antimicrobial effects of Aframomum

#### 5.3. Antidiabetic Activity

The seeds of A. melegueta are used in West Africa as a remedy for a variety of ailments such as stomachache, snakebite, and diarrhea, and have anti-inflammatory properties. Scholars conducted a 28-days subchronic toxicity study in male and female Sprague-Dawley rats to assess the safety of A. melegueta extracts. Dose-related increases in absolute and relative liver weights were observed at doses of 450 and 1500 mg/kg in both male and female rats with corresponding increases in alkaline acid enzymes and no signs of steatosis or cirrhosis. Blood glucose was reduced in male rats at the same dose [75]. Tetrapleura tetraptera and A. citratum fruits are used as spices and in the traditional pharmacopoeia of Cameroon. Researchers explored the phenolic profile of beverages made from such mixtures and their hypoglycemic activity against diabetic complications and found that their synergistic effect had optimal antihyperglycemic, hypoglycemic, triglyceride-lowering potentials and increased the activity of CAT, SOD, while decreasing the levels of Propanal and Hydrogen Peroxide [76]. Researchers explored the in vitro study of extracts of A. melegueta, A. danielli on  $\alpha$ -amylase,  $\alpha$ glucosidase, DPPH and SodiumNitroprusside (SNP)-induced lipid peroxidation in rat pancreas and the results showed that their inhibitory effects can be attributed to the presence of bioactive phytochemicals such as phenolic and some non-phenolic constituents. Moreover, these spices may exert their antidiabetic properties through mechanisms such as enzyme inhibition, free radical scavenging capacity and prevention of lipid peroxidation [77].

A study was conducted to evaluate the antidiabetic effects of an ethyl acetate extract of *A. melegueta* in a rat model of type 2 diabetes (T2D). Type 2 diabetes was induced in rats by two consecutive weeks of ad libitum intake of 10% fructose solution followed by intraperitoneal injection of streptozotocin (40 mg/kg) and animals were orally administered 150 or 300 mg/kg body weight of the extract daily. The results of the experiment showed that blood glucose, serum fructosamine, lactate dehydrogenase (LDH), creatine kinase isoenzymes (CK-MB), serum lipohepatic glycogen, insulin resistance, A1, CRI was higher in untreated diabetic animals than in normal animals. While serum insulin, pancreatic B-cell function (HOMA-B) and glucose tolerance were lower than normal animals. And the effect was more pronounced at 300 mg/kg body weight compared to 150 mg/kg body weight [78]. In another study, three aromatic alkanes, 6-paradol, 6-shogaol, and 6-gingerol, as well as a triterpenoid oleanolic acid, were isolated from *A. melegueta* fruits. The results of the study showed that all the compounds inhibited a-amylase and a-glucosidase, which may be responsible for the antidiabetic activity of *A. melegueta* fruits [15].

# 5.4. Anti-inflammatory Effect

The ethanol extract of *A. pruinosum* seeds was found to be therapeutically effective in rats with stroke and its associated motor and cognitive deficits. Stroke models were prepared using middle cerebral artery occlusion (MCAO) and bilateral common carotid artery occlusion (BCCAO). The results showed that MCAO induced cerebral infarction and increased lipid peroxidation, TNF- $\alpha$  and IL-1 $\beta$  levels. *A. pruinosum* enriched with nerolidol prevented these changes in a dose-dependent manner. BCCAO impairs nerve function, mobility and muscle strength in rats. It also increases lipid peroxidation and inflammatory cytokines in the cerebellum [79]. In addition, *A. pruinosum* methanolic extract showed some inhibitory effect on peptic ulcer. It was able to significantly reduce

the percentage of ulcer area from  $8.15\pm0.33\%$  to  $1.71s\ 0.44\%$  (500 mg/kg) and significantly increase the gastric production of mucus and nitric oxide,  $4.44\pm1.35$  and  $965.81\pm106.74 \ \mu$ mol/g (500 mg/kg), respectively (p<0.05) [80].

*A. melegueta* exerted a protective effect in CCI<sub>4</sub>-induced liver injury in rats, which may be attributed to the increased antioxidant defense potential, inhibition of inflammatory responses and hepatic tissue apoptosis such as elevated Alanine transaminase (ALT), thiobarbituric acid reactive substances (TBARS), tumor necrosis factor (TNF- $\alpha$ ), interleukin (IL)-1 $\beta$ , and caspases 3 and 9, and elevated hepatic glutathione [55] levels induced by CCI<sub>4</sub> intoxication [18]. Ilic et al. used bioactivity-guided isolation to show that the anti-inflammatory activity of ethanolic extracts of *A. melegueta* is due in part to inhibition of cyclooxygenase-2 (COX-2) enzyme activity and pro-inflammatory gene expression [81]. Summarize 5.3-5.4 section in Figure 6.

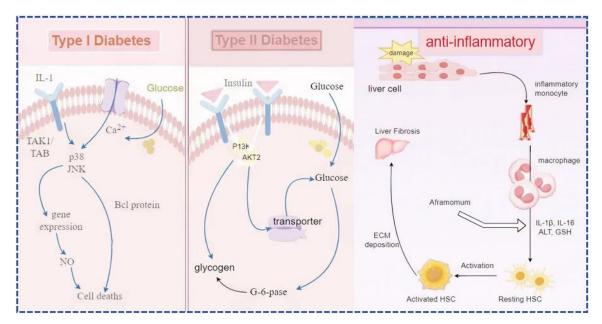


Figure 6. Antidiabetic and anti-inflammatory effects of Aframomum

#### 5.5. Ejaculatory Dysfunction

Hypothyroidism is thought to cause sexual dysfunction, such as ejaculatory disorders. *A. melegueta* is an aphrodisiac plant with ejaculatory-promoting effects. Scholars have investigated the protective effects of the aqueous (AE) and methanolic (ME) extracts of *A. melegueta*. The extracts increased testosterone levels (AE, ME 100 mg/kg) and lowered lactotropin levels (AE, 100 mg/kg; ME, 20 mg/kg) in comparison to the corresponding controls [82]. In addition, extracts of *A. melegueta* significantly shortened the ejaculatory latency and post-ejaculatory interval in rats. In spinal rats, mechanical or pharmacological stimuli triggered fictitious ejaculation, suggesting an ejaculation-promoting effect (p<0.05) [83]. Also, the extract of *A. melegueta* increased the secretion of testosterone in serum and testes, epididymis and seminal vesicles of mature male albino Wistar rats with gonadotropic effects [84]. Studies have shown that *A. melegueta* and *A. danielli* seeds can improve sexual- Practical role in folk medicine, inhibition of the activity of key enzymes associated with erectile dysfunction by some of their alkaloidal constituents may be a potential mechanism for

the induction of erectile function by these plants in folk medicine [22]. *A. melegueta* was also found to increase penile erection index, penetration and ejaculation frequency. The results of these studies suggest that *A. melegueta* may alter the sexual behavior of male rats by increasing sexual arousal [85].

#### 5.6. Liver Function Effect

Ethanol-induced oxidative stress appears to be one of the mechanisms of ethanol-induced liver injury. Sarah et al. explored the protective effects of a water-soluble plant extract of *A. melegueta* against ethanol-induced toxicity. It was found that co-administration of its extract inhibited elevated lipid peroxidation, restored reduced glutathione, and enhanced superoxide dismutase activity. These results highlight the ability of *A. melegueta* to attenuate oxidative damage in the liver, and the observed effects are related to its antioxidant activity [86]. Alcoholic extract of *A. citratum* reduced hepatic fat accumulation in high-fat diet (HFD)-induced obese C57BL/6 mice and was able to result in reduced liver weight and decreased liver and plasma lipid content [87].

#### 5.7. Blood Pressure and Lipids Lowering Effects

Ethanolic extracts of two plants (*A. melegueta, M. oleifera*) were prepared by Soxhlet extraction method and acute toxicity studies of both extracts were determined in rats using Lorke's method. The results showed that the combination treatment of 500 mg/kg *A. melegueta* and 500 mg/kg Moringa oleifera produced the best lipid-lowering effect. Also liver function tests showed no toxic effect of the two plants on hepatocytes at doses of 250 mg/kg and 500 mg/kg, thus confirming the hepatoprotective effect of the two herbs at the administered doses [88]. *A. melegueta* seeds have been reported to be used in folk medicine for the treatment of hypercholesterolemia and hypertension, and the results showed that *A. melegueta* has lipid-regulating, blood pressure-improving, hepatotoxicity-reducing and anti-hyperlipidemic effects [26].

## 5.8. Cytotoxic Effects

Kuete et al. evaluated the cytotoxicity of methanolic extracts of four *Aframomum* plants (*A. arundinaceum*, *A. alboviolaceum*, *A. kayserianum* and *A. polyanthum*) against nine sensitive and multidrug resistance (MDR) cancer cells. Preliminary experiments on leukemia CCRF-CEM cells at 40  $\mu$ g/mL showed that compounds extracted from *A. kayserianum* and *A. alboviolaceum* were less active and induced more than 50% growth of this cell line. The cytotoxic potential of *Aframomum* species was demonstrated and could be explored in more detail in the future for the development of novel anticancer drugs targeting sensitive and resistant phenotypes [89].

The ethanol extract of *A. angustifolium* seeds was found to be protective against some of the adverse side effects of 7,12-dimethylbenzanthracene (DMBA)-induced mammary cancer in female Wistar rats. Ethanol extract at a dose of 300 mg/kg body weight reduced serum estradiol levels, thereby preventing tretinoin-induced uterine hyperplasia. The extract prevented metabolic disorders by increasing body weight, decreasing triglyceride and total cholesterol levels and prevented lipid accumulation in the liver at both doses. In liver and kidney, catalase activity and TBARS levels were improved. Improvements in plasma activities of transaminases, alkaline phosphatase and uric acid levels were also observed [90]. Further, recent studies have shown that extracts of plants of the genus

*Aframomum* can be used as effective therapeutic inhibitors of depositary and mammalian rapamycin in renal cancer cells [91].

# 5.9. Copulation Effect

The aqueous extract of *A. danielli* seeds was found to have a positive effect on the bioactivity of mating performance in testis deficient rats. Mating insertion and ejaculation latency and frequency were significantly reduced and mean mating interval was significantly increased at 100 and 400 mg/kg doses (p<0.05). These findings suggest that the aqueous extract of *A. danielli* seeds enhances sexual potential and libido in large testicular insufficient males [92]. Furthermore, *A. melegueta* was found to show anti-estrogenic activity [19].

### 5.10. Others

A study showed that *A. melegueta* ethanolic seed extract at 25 and 50 mg/kg significantly reduced immobility time and prevented lack of interest and anxiety-like behaviors induced by unpredictable chronic mild stress (UCMS) in a forced swim test in mice (p<0.05), suggesting antidepressant potential. The extract reduced UCMS-induced malondialdehyde levels and increased glutathione concentrations in mice [93]. In addition, it has been shown that the seeds of *A. melegueta* have anti-obesity effects. The mechanism of its action may be related to the expression of genes associated with fatty acid synthesis, lipid transport, and adipocyte differentiation [94]. While another study found that *A. melegueta* extract and 6-gingerol exerted their anti-obesity effects mainly through activating the brown adipose tissue-sympathetic nervous system in the interscapular region [20]. Moreover, *A. melegueta* has also been used for pain relief, with oral doses of *A. melegueta* at 40 mg/kg and 80 mg/kg showing analgesic potential but affecting IL-6 levels, IL-1 $\beta$  and platelet-larger cell ratio (P-LCR) [95]. Summarize 5 sections in Table 4.

Extract(s)/compounds	Models	Dose	Effects/mechanisms	Ref
Antioxidant effect				
extraction of phenolic compounds	bovine serum albumin	0.25, 2.5, 25, 250 mg/mL	DPPH, FRAP, 5-LOX↓	[42]
extraction of <i>A. danielli</i> and <i>A. melegueta</i>	wistar strain albino rats	0-1200 µg/mL	MDA, DPPH, ABTS↓ Fe <sup>3+</sup> →Fe <sup>2+</sup>	[31]
extraction of <i>A. melegueta</i>	male Wistar albino rats	25, 50, 100, 200, 400 μg/mL	SOD, CAT↑, TBARS↓	[44]
extraction of A. citratum		0.25, 2.5, 25, 250 mg/mL	TPP、TFLV↑	[50]
ethanol and methanol extracts of <i>A. melegueta</i>	rats	20, 40, 60, 80, 100 μg/mL	DPPH, FRP, NO, $H_2O_2\downarrow$	[47]
A. Melegueta's seed extract	albino rats	50-200 mg/kg	MDA↓	[48]

Table 4. Pharmacological effects of Aframomum genus

ethanolic seed extract of A.	tochemistry and pharma male sprague-dawley		GSH, SOD↑	
melegueta	rats	10-100 µg/mL	MOD, nitrite↓	[56]
alcohol extract of <i>A. melegueta</i> seeds	wister albino male rats	200 mg/kg	DPPH, H <sub>2</sub> O <sub>2</sub> , OH <sup>-</sup> , SOD, GSH-Px, G6PD↓	[58]
Antimicrobial effect				
6-paradol, 8-gingerol and rac- 6-dihydroparadol	Mycobacterium smegmatis	64 mg/L	MIC values in the range 32- 64 mg/L	[16]
3-deoxyaulacocarpin A	Plasmodium falciparum	1.73 μg/mL	IC <sub>50</sub> =4.97 μM	[28]
aframodial, coronarin B, galanolactone	Plasmodium falciparum	3.13-200 μg/mL	IC <sub>50</sub> =24-56 μM	[27]
aframodial	Cryptococcus neoformans, Staphylococcusaureus, S. aureus	20-50 µg/mL	IC <sub>50</sub> /MIC= 6.0/20, 10/20 and 10/20 $\mu$ g/mL	[29]
3-(S)-acetyl-1-(4',5'- dihydroxy-3'-methoxy- phenyl)-7-(3",4"- dihydroxyphenyl) heptane, 6- paradol, 6-shogaol, 8-gingerol, dihydro-6-paradol	Staphylococcus aureus	50 µg/mL	The inhibition rates were 60.58%, 50%, 70.07%, 85.4%, and 59.85%	[14]
nerolidol, geraniol, α-terpinene	Staphylococcus aureus	1, 2, 4, 8, 16, and 32 mg/mL	inhibitory concentration 1 mg/mL	[63]
essential oil of <i>A. sceptrum rhizome</i>	Trypanosoma brucei brucei, Trichomonas vaginalis	50 µg/mL	mLC=1.51, 1.72 μL/mL	[65]
A. melegueta leaf and seed	Sitotroga cerealella	0.1, 0.2, 0.4, 0.6 and 0.8 g	40.33-100 %	[73]
4-shogeol	Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae and Serratia marcescens	1% v/v	0.4, 0.4, 0.2, and 0.4 mg/mL, respectively.	[66]
A. chrysanthum seeds	Staphylococcus aureus, Candida albicans and Trichophyton rubrum.	200, 100, 50, 25, 12.5 and 6.25 mg/mL	17.33±1.70, 10.67±0.47 and 10.67±1.63 mm	[67]
A. meleguet	Fusariumoxysporium, Penicillium sp	70, 100%	suppression ring of 11.5-15.5 mm	[68]

essential oil of A. danielli	Trypanosma brucei		$IC_{50} = 7.65 \mu g/mL$	[74]
Antidiabetic				
seeds of A. melegueta	sprague dawley rats	450 and 1500 mg/kg	liver alkaline phosphatase, aspartate aminotransferase↑ CAT, SOD↑	[75]
A. citratum fruits	rats	250 mg/kg	decreasing the levels of propanal and hydrogen peroxide	[76]
ethyl acetate extract of <i>A</i> . <i>melegueta</i>	type 2 diabetic rats	150, 300 mg/kg	LDH, CK-MB, serum lipohepatic glycogen, HOMA-IR, A1, CRI↑	[78]
6-paradol, oleanolic acid	α-amylase α-glucosidase	30, 60, 120 and 240 μg/mL	$\alpha$ -glucosidase (IC <sub>50</sub> :40.44 ± 5.77 μg/mL) $\alpha$ -amylase (IC <sub>50</sub> :68.69 ± 6.05 μg/mL)	[15]
Anti-inflammatory effect				
ethanol extract of <i>A</i> . <i>pruinosum</i> seeds	rats	75, 150, 300 mg/kg	TNF-α, IL-1β↑	[79]
methanol extract of <i>A</i> . <i>pruinosum</i>	male rats	500 mg/kg	percentage increase (Mucus and NO): $4.44 \pm 1.35$ and $965.81 \pm 106.74 \mu \text{mol/g}$	[80
A. melegueta	rats	1.3 g/kg	ALT, TBARS, TNF-α, IL- 1β, caspase3, 9↑	[18
Ejaculatory dysfunction				
water and methanol extracts of <i>A. melegueta</i>	rats	100 mg/kg	increased testosterone levels decreased lactin levels	[82
extracts of A. melegueta	adult wistar rats	20, 100 mg/kg	shortened ejaculatory latency	[83
water extracts of <i>A</i> . melegueta	mature male albino wistar rats	115, 230 mg/kg	secretion of epididymis and seminal vesicles↑	[84
Liver function				
water extracts of A. melegueta	male wistar rats	4.8 g/kg	MDA, SOD, GSH-Px↑	[86
hydroethanolic extracts of <i>A</i> . <i>citratum</i>	C57BL/6 mice	100, 200 mg/kg	liver weight and lipid content↓	[87
Lowering blood pressure and	blood lipids			
ethanol extract of <i>A. melegueta</i>	male qlbino wistar rats	250, 500 mg/kg	TC, TG, LDL-C↓	[17

#### Anti-tumor effects

methanol extract of <i>A</i> . <i>arundinaceum</i> , <i>A. alboviolaceum</i> , <i>A. kayserianum</i> ,	CCRF-CEM cell	40 µg/mL	IC <sub>50</sub> with 5.62-12.21 $\mu$ g/mL	[89]
A. polyanthum ethanol extract of A. angustifolium seeds	female wistar rats	300 mg/kg	H₂O₂, TBARS↓	[90]
Others				
Antidepressant - ethanolic seed extract of <i>A. melegueta</i>	mice	25, 50 mg/kg	MDA↓, GSH↑	[93]
Analgesic - A. melegueta	adult male Wistar rats	40, 80 mg/kg	IL-6, IL-1β, TNFx, P-LCR↑	[95]
<b>Cardiac fibrosis</b> - seed extract of <i>A. pruinosum</i>	rats	37.5, 75, 150 mg/kg	down regulate the expression of ANP	[96]

# 6. Applications

#### 6.1. Clinical

In a prospective, placebo-controlled, double-blind study, 57 outpatient women (45-65 years old) with menstrual problems associated with menopausal syndrome were recruited. The women were randomized into two groups, one receiving a plant combination treatment (250 mg per day in two divided doses) and the other receiving a placebo treatment for eight weeks. Health-related quality of life was assessed using the Cervantes scale at the beginning and end of the study. Patients treated with the plant extracts showed significant improvement in overall health-related quality of life scores compared to the placebo group. In contrast, there were no significant changes in the domains of the Cervantes Scale related to psychology, sexuality, and couple relationships (p<0.05) [97]. Inegbenebor et al. used in vivo animal studies to assess the health risks or benefits of *A. melegueta* in pregnant women. The results showed that rats fed *A. melegueta* did not give birth at all, suggesting that high intake of *A. melegueta* poses a health risk to women in the first trimester of pregnancy [98].

The researchers evaluated the effect of a natural mixture of *A. angustifolium* seed extract containing labdanum diterpenoids on these aging markers. The experimental results showed that the extract had a strong modifying effect on the gene expression profile of treated normal human keratinocytes but a weaker modifying effect on normal human fibroblasts, suggesting that its seed extract has a potential role against skin aging [99]. Increasing adaptive thermogenesis through activation of brown adipose tissue (BAT) is a promising and practical strategy for preventing obesity and related diseases. Ingestion of a single dose of 40 mg of Paradise (*A. melegueta*) extract has been reported to trigger BAT thermogenesis in individuals with high BAT activity, but not in individuals with low BAT activity. In the study, subjects ingested Paradise extract (40 mg/day) or placebo daily for 5 weeks. Whole-body resting energy expenditure under thermoneutral conditions remained unchanged in subjects after Paradise extract treatment. However, post-treatment chemotherapy-induced thrombocytopenia (CIT) was significantly higher in the Paradise extract-treated group than

in the placebo-treated group. Notably, percentage body fat decreased slightly but significantly after Paradise extract treatment, whereas it did not decrease after placebo treatment. These results suggest that Paradise-enhanced BAT-dependent adaptive thermogenesis has the potential to reduce body fat content in humans (p<0.05) [99]. Ottu et al. showed that Aframomum melegueta contains bioactive compounds with strong potential to act as ERK5 inhibitors, providing a new approach to breast cancer treatment [100]. Seed extract of A. melegueta activated Transient Receptor Potential Vanilloid 1 (TRPV1), modulated 5-HT1A receptor and inhibited Fatty acid amide hydrolase (FAAH). It reduces anxiety and stress-related tension, improves overall mood, improves sleep quality, and has no reported side effects [101]. Summarize this section in Figure 8.

# 6.2. Economics

Ethanolic and aqueous extracts of *A. melegueta* from Nigeria inhibited the growth of fungi isolated from spoiled okro on agar plates (*Botryodiplodia theobromae, Aspergillus niger, Aspergillus flavus, Mucor sp., Rhizopus stolonifer, Penicillium sp.* and *Fusarium sp.*) with an average minimum inhibitory concentration of 6.0%. In the applied treatments, the mixture of *A. melequeta* extracts significantly reduced the biodegradation of fresh okro, with little loss of carbohydrates (1.2%) after 3 months of storage, which may be economically important in the application of threshold technology for fruit preservation (p<0.05) [102]. In addition, findings suggest that combinations of *A. melegueta* seeds could also be used in food and nutritional supplements for erectile function [103].



Figure 7. Aframomum applications in health and economy.

The study found that the decline in yield of korarima (*A. corrorima*) was mainly due to the destruction of the plant's natural habitat. A survey was conducted in three major korarima growing administrative areas in southern Ethiopia, a total of three different local varieties named korarima were recorded and individual farms ranged from one to three indicating low on-farm biodiversity. More households cultivated in Gamo Gofa and Kaffa and only a few households cultivated korarima. The results of this study suggest that maintenance of shade trees on the main farmLand is a major

requirement for korarima production [104].

When the spice *A. danielli* was ground into material and used to store corn and soybeans under specific environmental conditions, i.e., at a temperature of  $26 \pm 1$  °C and a relative humidity of  $75 \pm 5\%$ , the results showed that mold and insect damage could be effectively controlled, and that this good storage condition could be sustained for up to 15 months, suggesting that *A. danielli* may be useful as a natural preservative [105].

# 7. Conclusion and Perspectives

*Aframomum* is a group of plants with great potential. Studies conducted so far have revealed its rich chemical constituents including volatile oils, phenolic compounds, flavonoids and lignans. These constituents have various pharmacological effects such as antibacterial, antioxidant, analgesic and anti-inflammatory. Its traditional uses in African medicine and food have laid the foundation for further exploration. However, studies on its chemical composition and pharmacology are still incomplete, and although in vitro and some in vivo studies have shown promise, a comprehensive understanding of its mechanism of action and therapeutic potential is still incomplete.

Prospect: Particular attention needs to be paid to resource conservation, in-depth development of active ingredients and exploration of mechanisms. Collect and conserve wild Aframomum germplasm resources from different geographic populations, and establish live and seed banks. Species-specific molecular markers should be developed using genome sequencing technologies (e.g., RAD-seq for simplified genome sequencing) to assist in classification and genetic diversity assessment. Different parts of Aframomum spp, such as roots, stems, leaves, flowers and fruits, as well as different growing environments, should be studied in depth, and more new compounds, especially those with unique structures and biological activities, should be discovered with the help of modern isolation techniques and structure identification methods. In-depth study of the molecular mechanisms of their pharmacological effects is essential. Understanding how bioactive compounds interact with cellular targets and signaling pathways will help develop more targeted therapies. Techniques such as proteomics and genomics can be utilized in future studies to determine the specific mechanism of effect exerted by Aframomum, thereby revealing its mode of action. In addition, given its potential as a spice and medicinal plant, efforts should be made to develop related products. This includes the development of standardized extracts for the nutraceutical market, functional food ingredients or novel pharmaceutical formulations.

In summary, *Aframomum* is a plant resource with great potential, with a large number of novel compounds and medicinal properties that need to be studied in depth. However, there are currently insufficient studies, and in the future, it is necessary to strengthen the taxonomy, compositional analysis, and pharmacological mechanism of action studies of this genus, in order to provide a more solid foundation for the conservation, development and utilization of its resources.

# **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.

# Funding

This work was supported by the Science and Technology Innovation Talent System Construction Program of Shaanxi University of Chinese Medicine (2023-CXTD-05) and State Administration of Traditional Chinese Medicine high-level key discipline construction project (zyyzdxk-2023202).

# ORCID 回

Yezi Ma: 0009-0009-6279-5869 Haonan Xu: 0000-0001-8873-0320 Yu Sun: 0000-0001-5465-7989 Hao Fan: 0000-0002-0822-1639 Yuze Li: 0000-0001-7571-3214 Xiaomei Song: 0000-0003-1906-1578 Wei Wang: 0000-0002-4699-0498 Dongdong Zhang: 0000-0003-0956-1261

# References

- [1] L. J. Larsen K, Maas H, Maas P. (1998). Zingiberaceae, New York (NY): Springer 1, 474–495.
- [2] J. B. Dhetchuvi, A. H. Wortley and D. J. Harris (2011). A new species of *Aframomum* (Zingiberaceae) from Central Africa, *Phytotaxa* 28, 31-34.
- [3] T. S. Tane P, Ayimele GA and J.D. Conolly (2005). Bioactive metabolites from *Aframomum species*, *11th NAPRECA symposium book of proceed ings, Antananarivo, Madagascar* 1, 214-223.
- [4] G. Furo, A. Manaye and A. Negasa (2019). Identification of spice shade and support tree species, South Western Ethiopia, *Agroforest. Syst.* 94, 95-102.
- [5] B. Mekassa and B. S. Chandravanshi (2015). Levels of selected essential and non-essential metals in seeds of korarima (*Aframomum corrorima*) cultivated in Ethiopia, *Braz. J. Food Technol.* 18, 102-111.
- [6] K. M. Kafoutchoni, R. Idohou, A. Egeru, K. V. Salako, C. Agbangla, A. C. Adomou and A. E. Assogbadjo (2018). Species richness, cultural importance, and prioritization of wild spices for conservation in the Sudano-Guinean zone of Benin (West Africa), *J. Ethnobiol. Ethnomed.* 14, 67. DOI:10.1186/s13002-018-0267-y
- [7] A. Sarpong and S. Abugre (2020). The potential of domesticating grains of paradise (*Aframomum melegueta*), a non-timber forest product in off-reserve tree farms, *J. Sustain. Forest.* **41**, 159-172.
- [8] T. Hailu, T. Haileselassie and T. Feyissa (2022). In vitro regeneration of Korarima (*Aframomum corrorima* (Braun) P. C. M. Jansen): a threatened spice and medicinal herb from Ethiopia, *Scientifica* 2022, 1-12.
- [9] S. Kinfu, T. Wato and T. Negash (2022). Study on character association and path analysis in Korarima (*Aframomum Corrorima* (Braun) Jansen) Germplasms at Jimma Southwestern, Ethiopia, *Heliyon* 8, e08812. DOI:10.1016/j.heliyon.2022.e08812
- [10] J. Amponsah, N. Adamtey, W. Elegba and K. E. Danso (2013). In situ morphometric characterization of *Aframomum melegueta* accessions in Ghana, *AoB. Plants.* 5, 1-12.

- [11] H. Tilahun, H. Teklehaimanot, G. Fekadu and F. Tileye (2022). Analyses of genetic diversity and population structure in cultivated and wild korarima [*Aframomum corrorima* (Braun) P. C. M. Jansen] populations from Ethiopia using inter simple sequence repeats markers, *J. Appl. Res. Med. Aromat. Plants.* **30**, 100386. DOI: 10.1016/j.jarmap.2022.100386
- [12] T. Hailu, T. Feyissa, A. Dekebo, G. Hailemichael and F. Gadissa (2021). Diversity in capsule and seed morphological and phytochemical features and essential oil composition of korarima (*Aframomum corrorima* (braun) P. C. M. jansen) collections from Ethiopia, *Biochem. Syst. Ecol.* 97, 104275. DOI:10.1016/j.bse.2021.104275
- [13] A. B. Abdel-Naim, A. A. Alghamdi, M. M. Algandaby, F. A. Al-Abbasi, A. M. Al-Abd, H. M. Abdallah,
   A. M. El-Halawany and M. Hattori (2017). Phenolics isolated from *Aframomum meleguta* enhance proliferation and ossification markers in bone cells, *Molecules* 22, 1467. DOI:10.3390/molecules22091467
- [14] R. S. El Dine, M. A. Elfaky, H. Asfour and A. M. El Halawany (2019). Anti-adhesive activity of *Aframomum melegueta* major phenolics on lower respiratory tract pathogens, *Nat.Prod. Res.* 19, 1585843. DOI:10.1080/14786419.2019.1585843
- [15] A. Mohammed, V. A. Gbonjubola, N. A. Koorbanally and M. S. Islam (2017). Inhibition of key enzymes linked to type 2 diabetes by compounds isolated from *Aframomum melegueta* fruit, *harm. Biol.* 55, 1010-1016.
- [16] B. Gröblacher, V. Maier, O. Kunert and F. Bucar (2012). Putative mycobacterial efflux inhibitors from the seeds of *Aframomum melegueta*, J. Nat. Prod. 75, 1393-1399.
- [17] Z. Zhang, F. Zulfiqar, Z. Ali and I. A. Khan (2020). Two undescribed paradol-related specialized metabolites from *Aframomum melegueta*, *Nat. Prod. Res.* 35, 3707-3713.
- [18] A. M. El-Halawany, R. S. El Dine, N. S. El Sayed and M. Hattori (2014). Protective effect of *Aframomum melegueta* phenolics against CCl<sub>4</sub>-induced rat hepatocytes damage; role of apoptosis and proinflammatory cytokines inhibition, *Sci. Rep.* 4, 5880. DOI:10.1038/srep05880
- [19] A. M. El-Halawany and M. Hattori (2012). Anti-oestrogenic diarylheptanoids from *Aframomum melegueta* with in silico oestrogen receptor alpha binding conformation similar to enterodiol and enterolactone, *Food Chem.* 134, 219-226.
- [20] H. Hattori, K. Yamauchi, S. Onwona-Agyeman and T. Mitsunaga (2018). Identification of vanilloid compounds in the Grains of Paradise and their effects on sympathetic nerve activity, *J. Sci. Food Agric.* 98, 4742-4748.
- [21] P. Escoubas, L. Lajide and J. Mizutani (1995). Termite antifeedant activity in Aframomum melegueta, Phytochemistry 4, 1097-1099.
- [22] S. A. Adefegha, G. Oboh, B. M. Okeke and S. I. Oyeleye (2017). Comparative effects of alkaloid extracts from *Aframomum melegueta* (*Alligator Pepper*) and *Aframomum danielli* (*Bastered Melegueta*) on enzymes relevant to erectile dysfunction, J. Diet. Suppl. 5, 542-552.
- [23] P. Kamnaing, A. Tsopmo, E. A. Tanifum, M. H. K. Tchuendem, P. Tane, J. F. Ayafor, O. Sterner, D. Rattendi, M. M. Iwu, B. Schuster and C. Bacchi (2003). Trypanocidal diarylheptanoids from *Aframomum letestuianum*, J. Nat. Prod. 66, 364-367.
- [24] J. F. Ayafor, M. H. K. Tchuendem, B. Nyasse, F. Tillequin and H. Anke (1994). Aframodial and other bioactive diterpenoids from *Aframomum* species, *Pure Appl. Chem.* 66, 2327-2330.
- [25] M. Marlier, G. L. Guellec, G. Lognay, J. P. Wathelet and M. Severin (1993). Characterization of three labdane diterpenes from *Aframomum alboviolaceum*, *Planta Med.* 59, 455-457.
- [26] S. A. Adefegha, G. Oboh, O. M. Adefegha and T. Henle (2016). Alligator pepper/Grain of Paradise

(*Aframomum melegueta*) modulates angiotensin-I converting enzyme activity, lipid profile and oxidative imbalances in a rat model of hypercholesterolemia, *Pathophysiology* **23**, 191-202.

- [27] G. Duker-Eshun, J. W. Jaroszewski, W. A. Asomaning, F. Oppong-Boachie, C. E. Olsen and S. B. Christensen (2002). Antiplasmodial activity of labdanes from *Aframomum latifolium* and *Aframomum sceptrum*, *Planta Med.* 68, 642-644.
- [28] M. Kenmogne, E. Prost, D. Harakat, M. Jacquier, M. Frederich, L. Sondengam, M. Zeches and P. Waffoteguo (2006). Five labdane diterpenoids from the seeds of *Aframomum zambesiacum*, *Phytochemistry* 67, 432-438.
- [29] S. J. N. Tatsimo, P. Tane, J. Melissa, B. L. Sondengam, C. O. Okunji, B. M. Schuster, M. M. Iwu and I. A. Khan (2006). Antimicrobial principle from *Aframomum longifolius*, *Planta Med.* 72, 132-135.
- [30] J. F. Ayafor, M. H. Tchuendem, B. Nyasse, F. Tillequin and H. Anke (1994). Novel bioactive diterpenoids from *Aframomum aulacocarpos*, J. Nat. Prod. 57, 917-923.
- [31] S. A. Adefegha and G. Oboh (2012). Acetylcholinesterase (AChE) inhibitory activity, antioxidant properties and phenolic composition of two *Aframomum* species, *J. Basic Clin. Physiol. Pharmacol.* 24, 153-161.
- [32] D. F. Dibwe, S. Awale, H. Morita and Y. Tezuka (2015). Anti-austeritic constituents of the congolese medicinal plant *Aframomum melegueta*, *Nat. Prod. Commun.* 10, 997-999.
- [33] A. Tsopmo, G. A. Ayimele, P. Tane, J. F. Ayafor, J. D. Connolly and O. Sterner (2002). A norbislabdane and other labdanes from *Aframonum sulcatum*, *Tetrahedron* 58, 2725-2728.
- [34] Z. Cheikh-Ali, T. Okpekon, F. Roblot, C. Bories, M. Cardao, J. C. Jullian, E. Poupon and P. Champy (2011). Labdane diterpenoids from *Aframomum sceptrum*: NMR study and antiparasitic activities, *Phytochemistry Lett.* 4, 240-244.
- [35] C. Tomla, P. Kamnaing, G. A. Ayimele, E. A. Tanifum, A. Tsopmo, P. Tane, J. F. Ayafor and J. D. Connolly (2002). Three labdane diterpenoids from *Aframomum sceptrum* (Zingiberaceae), *Phytochemistry* 60, 197-200.
- [36] S. V. T. Sob, P. Tane, B. T. Ngadjui, J. D. Connolly and D. Ma (2007). Trypanocidal labdane diterpenoids from the seeds of *Aframomum aulacocarpos* (Zingiberaceae), *Tetrahedron* 63, 8993-8998.
- [37] H. K. Wabo, P. Tane and J. D. Connolly (2006). Diterpenoids and sesquiterpenoids from Aframomum arundinaceum, Biochem. Syst. Ecol. 34, 603-605.
- [38] J. F. Ayafor and J. D. Connolly (1981). 2R,3R-(+)-3-acetoxy-4',5-dihydroxy-7- methoxyflavanone and 2R,3R-(+)-3-acetoxy-4',5,7-trihydroxyflavanone: two new 3-acetylated dihydroflavonols from Aframomum pruinosum Gagnepain (Zingiberaceae), J. Chem. Society, Perkin Transactions. 1, 2563-2565.
- [39] G. Vidari, P. V. Finzi and M. Bernardi (1971). Flavonols and quinones in stems of Aframomum giganteum, Phytochemistry 10, 3335-3339.
- [40] U. E. Olunkwa, K. M. E. Iheanacho, C. U. Igwe, L. A. Nwaogu and J. N. Iheanacho (2023). Bioactive component analysis of aqueous seed extract of *Aframomum melengueta*, *GSC Bio. Pharm. Sci.* 25, 249-272.
- [41] H. Ene-Obong, N. Onuoha, L. Aburime and O. Mbah (2017). Chemical composition and antioxidant activities of some indigenous spices consumed in Nigeria, *Food Chem.* 238, 58-64.
- [42] E. Manga, Y. Brostaux, J. L. Ngondi and M. Sindic (2020). Optimisation of phenolic compounds and antioxidant activity extraction conditions of a roasted mix of *Tetrapleura tetraptera* (Schumach & Thonn.) and *Aframomum citratum* (C. Pereira) fruits using response surface methodology (RSM), *Saudi J. Biol. Sci.* 27, 2054-2064.

- [43] T. A. Sokamte, P. D. Mbougueng, N. L. Tatsadjieu and N. M. Sachindra (2019). Phenolic compounds characterization and antioxidant activities of selected spices from Cameroon, S. Afri. J. Bot. 121, 7-15.
- [44] S. O. Onoja, Y. N. Omeh, M. I. Ezeja and M. N. Chukwu (2014). Evaluation of the in vitro and in vivo antioxidant potentials of *Aframomum melegueta* methanolic seed extract, *J. Trop. Med.* 2014, 159343. DOI: 10.1155/2014/159343
- [45] F. Oboh and J. Imafidon (2018). Antioxidant and sensory properties of new beverage formulations composed of *Palm sugar*, *Aframomum melegueta*, and Citric acid, *Beverages* 4, 59. DOI: 10.3390/beverages4030059
- [46] G. O. Adegoke, O. Makinde, K. O. Falade and P. I. Uzo-Peters (2003). Extraction and characterization of antioxidants from *Aframomum melegueta* and *Xylopia aethiopica*, *Eur. Food Res. Technol.* 216, 526-528.
- [47] M. Latif, I. Elkoraichi, O. El Faqer, H. Wahnou, R. Elaje, E. M. Mtairag, M. Oudghiri and S. Rais (2024). *Aframomum melegueta*: evaluation of chronic toxicity, HPLC profiling, and in vitro/in vivo antioxidant assessment of seeds extracts, *Chem. Biodivers.* 13, 202400942. DOI: 10.1002/cbdv.202400942
- [48] S. Umukoro and B. R. Ashorobi (2007). Further pharmacological studies on aqueous seed extract of *Aframomum melegueta* in rats, J. Ethnopharmacol. 115, 489-493.
- [49] S. C. D. Meffo, G. S. S. Njateng, J. D. D. Tamokou, P. Tane and J. R. Kuiate (2019). Essential oils from seeds of *Aframomum citratum* (C. Pereira) K. Schum, *Aframomum daniellii* (Hook. F.) K. Schum, *Piper capense* (Lin. F) and *Monodora myristica* (Gaertn.) Dunal NL and their antioxidant capacity in a cosmetic cream, *J. Essent. Oil-Bear. Plant.* 22, 324-334.
- [50] E. Manga, M. Fauconnier, J. Ngondi, A. Ngando and M. Sindic (2020). In vitro biological activities of aqueous extracts of *Tetrapleura tetraptera* (Schumach. & Thonn.) taub. and *Aframomum citratum* (C. Pereira) K.Schum from three Agroecologic Zones in Cameroon, *Asian Pac. J. Trop. Med.* 13, 71-80.
- [51] E. Dessalegn, G. Bultosa, G. Haki, F. Chen and H. P. V. Rupasinghe (2021). Antioxidant and cytotoxicity to liver cancer HepG2 cells in vitro of Korarima (*Aframomum corrorima* (Braun) P.C.M. Jansen) seed extracts, *Int. J. Food Prop.* 25, 1-10.
- [52] E. E. Essien, P. S. Thomas, K. Oriakhi and M. I. Choudhary (2017). Characterization and antioxidant activity of volatile constituents from different parts of *Aframomum danielli* (Hook) K. Schum, *Medicines* 4, 29. DOI:10.3390/medicines4020029
- [53] H. Cronin and Z. D. Draelos (2010). Top 10 botanical ingredients in 2010 anti-aging creams, J. Cosmet. Dermatol. 9, 218-225.
- [54] H. Agnaniet, C. Menut and J. M. Bessière (2004). Aromatic plants of tropical central Africa. Part XLIX: chemical composition of essential oils of the leaf and rhizome of *Aframomum giganteum* K. Schum from Gabon, *Flavour Frag. J.* 19, 205-209.
- [55] Z. Liu, S. Liu, H. Shi, H. Ren, R. Wang, J. Yang and T. Guo (2015). Fluorescently labeled degradable thermoplastic polyurethane elastomers: Visual evaluation for the degradation behavior, *Inc. J. Appl. Polym. Sci.* **132**, 42519. DOI:10.1002/app.42519
- [56] I. Ishola, A. Awoyemi and G. Afolayan (2016). Involvement of antioxidant system in the amelioration of scopolamine-induced memory impairment by grains of Paradise (*Aframomum melegueta* K. Schum.) extract, *Drug Res.* 66, 455-463.
- [57] S. V. Luca, A. Trifan, G. Zengin, K. I. Sinan, A. I. Uba, I. Korona-Glowniak and K. Skalicka-Woźniak (2022). Evaluating the phyto-complexity and poly-pharmacology of spices: the case of *Aframomum melegueta* K. Schum (Zingiberaceae), *Food Biosci.* **49**, 101929. DOI:10.1016/j.fbio.2022.101929
- [58] N. S. Adigun, A. T. Oladiji and T. O. Ajiboye (2016). Antioxidant and anti-hyperlipidemic activity of

hydroethanolic seed extract of *Aframomum melegueta* K. Schum in Triton X-100 induced hyperlipidemic rats, *S. Afri. J. Bot.* **105**, 324-332.

- [59] E. I. L. Mounia, E. F. Othman, W. Hicham, E. Rajaa, M. El-Mostafa, O. Mounia and R. Samira (2025). *Aframomum Melegueta*: evaluation of chronic toxicity, HPLC profiling, and in vitro/in vivo antioxidant assessment of seeds extracts, *Chem. Biodivers.* 22, e202400942. DOI: 10.1002/cbdv.202400942
- [60] S. K. Nguikwie, M. A. Nyegue, F. N.-F. Belinga, R. A. N. Ngane, B. Romestand, A. Kouzayha, H. Casabianca, P. H. A. Zollo and C. Menut (2013). The chemical composition and antibacterial activities of the essential oils from three *Aframomum* species from cameroon, and their potential as sources of (E)-(R)-nerolidol, *Nat. Prod. Commun.* 8, 829-834.
- [61] N. E. S. Lale (1992). A laboratory study of the comparative toxicity of products from three spices to the maize weevil, *Postharvest. Biol. Technol.* 2, 61-64.
- [62] A. Martins, L. Salgueiro, M. Gonçalves, A. Cunha, R. Vila, S. Cañigueral, V. Mazzoni, F. Tomi and J. Casanova (2001). Essential oil composition and antimicrobial activity of three Zingiberaceae from S.Tomé e Príncipe, *Planta Med.* 67, 580-584.
- [63] G. Mulugeta, T. Huijun and Z. Yaping (2024). Response surface optimization for supercritical carbon dioxide extraction of Korarima (*Aframomum corrorima*) seed oil and its antibacterial activity evaluation, J. Supercrit. Fluids. 215, 106411. DOI: 10.1016/j.supflu.2024.106411
- [64] C. O. Nwonuma, T. A. Adelani-Akande, O. O. Osemwegie, A. F. Olaniran and T. A. Adeyemo (2019). Comparative study of the in vitro phytochemicals and antimicrobial potential of six medicinal plants, *F1000Research* 8, 81. DOI:10.12688/f1000research.17094.2
- [65] Z. Cheikh-Ali, M. Adiko, S. Bouttier, C. Bories, T. Okpekon, E. Poupon and P. Champy (2011). Composition, and antimicrobial and remarkable antiprotozoal activities of the essential oil of rhizomes of *Aframomum sceptrum* K. Schum. (Zingiberaceae), *Chem. Biodiver.* 8, 658-667.
- [66] A. E. Koshak, H. M. Okairy, M. A. Elfaky, H. M. Abdallah, G. A. Mohamed, S. R. M. Ibrahim, A. A. Alzain, M. Abulfaraj, W. A. H. Hegazy and S. I. Nazeih (2023). Antimicrobial and anti-virulence activities of 4-shogaol from grain of paradise against gram-negative bacteria: integration of experimental and computational methods, *J. Ethnopharmacol.* 323, 117611. DOI: 10.1016/j.jep.2023.117611
- [67] G. I. Ndukwe, O. I. Iyemeaikere and J. L. Konne (2021). Phytochemical analysis and antimicrobial activity of *Aframomum chrysanthum* seed extracts, *Int. J. Chem. Stud.* **9**, 14-20.
- [68] A. Patience Saturday, U. Eyoanwan Offon, W. Ebere Ifiokobong and I. Aniefon Alphonsus (2024). Assessing the antimicrobial activity of *Aframomum melegueta* and *Piper guineense* extract on pathogens of rot diseases of cucumber fruit, *bioRxiv-Microbiol.* 9, 614230. DOI: 10.1101/2024.09.21.614230
- [69] B. F. Oluwabamiwo, G. O. Adegoke, R. Akinoso and S. A. Denloye (2018). Control of aflatoxigenic mould and aflatoxins in melon seeds using *Aframomum danielli* indigenous plant, *Acta Hortic.* 69, 507-512.
- [70] G. O. Adegoke, S. B. Fasoyiro and B. Skura (2000). Control of microbial growth, browning and lipid oxidation by the spice *Aframomum danielli*, *Eur. Food Res. Technol.* 211, 342-345.
- [71] D. A. Ukeh, S. B. A. Umoetok, A. S. Bowman, A. Jennifer Mordue, J. A. Pickett and M. A. Birkett (2012). *Alligator pepper*, *Aframomum melegueta*, and *ginger*, *Zingiber officinale*, reduce stored maize infestation by the maize weevil, Sitophilus zeamais in traditional African granaries, *Crop Protection*. 32, 99-103.
- [72] D. A. Ukeh, M. A. Birkett, J. A. Pickett, A. S. Bowman and A. Jennifer Mordue (2009). Repellent activity of *Alligator pepper*, *Aframomum melegueta*, and *ginger*, *Zingiber officinale*, against the maize weevil, Sitophilus zeamais, *Phytochemistry* 70, 751-758.

- [73] A. C. Adeyemo, M. O. Ashamo and O. O. Odeyemi (2013). *Aframomum melegueta*: a potential botanical pesticide against Sitotroga cerealellain festation on two paddy varieties, *Arch. Phytopath. Plant.* 47, 1841-1851.
- [74] S. L. N. Kamte, F. Ranjbarian, G. D. Campagnaro, P. C. B. Nya, H. Mbuntcha, V. Woguem, H. M. Womeni, L. A. Ta, C. Giordani, L. Barboni, G. Benelli, L. Cappellacci, A. Hofer, R. Petrelli and F. Maggi (2017). Trypanosoma brucei Inhibition by essential oils from medicinal and aromatic plants traditionally used in Cameroon (*Azadirachta indica, Aframomum melegueta, Aframomum daniellii, Clausena anisata, Dichrostachys cinerea* and *Echinops giganteus*), *Int. J. Environ. Res. Public Health.* 14, 737. DOI: 10.3390/ijerph14070737
- [75] N. Ilic, B. M. Schmidt, A. Poulev and I. Raskin (2009). Toxicological evaluation of Grains of Paradise (*Aframomum melegueta*) [Roscoe] K. Schum, J. Ethnopharmacol. 127, 352-356.
- [76] M. Eyenga, N. G. R. Takuissu, A. Ziyyat, J. L. Ngondi and M. Sindic (2020). Hypoglycaemic activity of preheated (roasting) *Aframomum citratum* (C. Pereira) K. Schum and *Tetrapleura tetraptera* (Schumach Thonn.) fruits beverage on Streptozotocin-induced rats, *J. Pharmacogn. Phytotherapy* 12, 44-61.
- [77] S. A. Adefegha and G. Oboh (2012). Inhibition of key enzymes linked to type 2 diabetes and sodium nitroprusside-induced lipid peroxidation in rat pancreas by water extractable phytochemicals from some tropical spices, *Pharm. Biol.* 50, 857-865.
- [78] A. Mohammed, N. A. Koorbanally and M. S. Islam (2015). Ethyl acetate fraction of *Aframomum melegueta* fruit ameliorates pancreatic β-cell dysfunction and major diabetes-related parameters in a type 2 diabetes model of rats, *J. Ethnopharmacol.* 175, 518-527.
- [79] A. F. Goumtsa, E. P. Nguelefack-Mbuyo, C. K. Fofie, A. R. Fokoua, A. Becker and T. B. Nguelefack (2024). Neuroprotective effects of *Aframomum pruinosum* seed extract against stroke in rat: Role of antioxidant and anti-inflammatory mechanisms, *J. Stroke Cerebrovasc. Dis.* 33, 107942.
- [80] L. B. Kouitcheu Mabeku, B. Nanfack Nana, B. Eyoum Bille, R. Tchuenteu Tchuenguem and E. Nguepi (2017). Anti-Helicobacter pylori and antiulcerogenic activity of *Aframomum pruinosum* seeds on indomethacin-induced gastric ulcer in rats, *Pharm. Biol.* 55, 929-936.
- [81] N. M. Ilic, M. Dey, A. A. Poulev, S. Logendra, P. E. Kuhn and I. Raskin (2014). Anti-inflammatory activity of grains of Paradise (*Aframomum melegueta* Schum) extract, *J. Agr. Food Chem.* 62, 10452-10457.
- [82] F. X. Kemka Nguimatio, P. B. Deeh Defo, M. Wankeu-Nya, E. Ngadjui, A. Kamanyi, P. Kamtchouing and P. Watcho (2019). *Aframomum melegueta* prevents the ejaculatory complications of propylthiouracil-induced hypothyroidism in sexually experienced male rats: Evidence from intravaginal and fictive ejaculations, *J. Integrat. Med.* 17, 359-365.
- [83] P. Watcho, F. X. Kemka, P. B. Deeh Defo, M. Wankeu Nya, P. Kamtchouing and A. Kamanyi (2017). In/ex copula ejaculatory activities of aqueous and methanolic extracts of *Aframomum melegueta* (Zingiberaceae) in sexually experienced male rat, *Andrologia* 10, 1-9.
- [84] G. Y. F. Mbongue, P. Kamtchouing and T. Dimo (2011). Effects of the aqueous extract of dry seeds of *Aframomum melegueta* on some parameters of the reproductive function of mature male rats, *Andrologia* 44, 53-58.
- [85] P. Kamtchouing, G. Y. F. Mbongue, T. Dimo, P. Watcho, H. B. Jatsa and S. D. Sokeng (2002). Effects of *Aframomum melegueta* and *Piper guineense* on sexual behaviour of male rats, *Behav. Pharmacol.* 13, 243-247.
- [86] S. O. Nwozo and B. E. Oyinloye (2011). Hepatoprotective effect of aqueous extract of Aframomum

melegueta on ethanol-induced toxicity in rats, Acta Biochim. Pol. 58, 355-358.

- [87] A. P. Nwakiban Atchan, S. T. Shivashankara, S. Piazza, A. D. Tchamgoue, G. Beretta, M. Dell'Agli, P. Magni, G. A. Agbor, J.-R. Kuiaté and U. V. Manjappara (2022). Polyphenol-rich extracts of Xylopia and *Aframomum* Species show metabolic benefits by lowering hepatic lipid accumulation in diet-induced obese mice, *ACS Omega*. 7, 11914-11928.
- [88] L. U. Nwankwo, F. A. Onyegbule, C. C. Abba and E. Agbamu (2022). Comparative hypolipidemic evaluation of *Aframomum melegueta* seeds and *Moringa oleifera* leaves, *J. Pharm. Res. Int.* 33, 166-182.
- [89] V. Kuete, P. Y. Ango, S. O. Yeboah, A. T. Mbaveng, R. Mapitse, G. D. W. F. Kapche, B. T. Ngadjui and T. Efferth (2014). Cytotoxicity of four *Aframomum* species (*A. arundinaceum, A. alboviolaceum, A. kayserianum and A. polyanthum*) towards multi-factorial drug resistant cancer cell lines, *BMC Complement. Altern. Med.* 14, 340. DOI: 10.1186/1472-6882-14-340
- [90] I. Makamwe, F. R. Ntentie, M. A. A. Mbong, A. P. N. Kengne, H. M. F. Tienoue, G. R. N. Takuissu, U. A. N. Onsi, S. Zingue and J. E. Oben (2023). The ethanolic extract of *Aframomum angustifolium* seeds protects against tamoxifen-induced side effects in rats with breast cancer, *Adv. Trad. Med.* 24, 449-458.
- [91] O. O. Elekofehinti, P. A. Ajiboro, M. O. Akinjiyan, T. P. Saliu, F. O. Ayodeji, F. M. Ojo and C. Oluwamodupe (2023). Identification of natural inhibitor from *Aframomum melegueta* targeting survivin and mammalian rapamycin signaling pathway in kidney cancer, *Inform. Med. Unlocked.* 41, 101320. DOI: 10.1016/j.imu.2023.101320
- [92] N. Zacharie, M. L. Dieudonné, W. N. Modeste, N. M. Ide, K. B. Landry, B. Emma, E. Noël, M. Armel, T. Yebga, M. P. V. G and N. N. D. Camille (2020). Potential activity of *Aframomum daniellii* (Zingiberaceae) dry seeds: a case study of its action mechanism on the Wistar rat strain with testicular deficiency, *Biomed. Pharmacother.* **131**, 110759. DOI: 10.1016/j.biopha.2020.110759
- [93] E. T. Ojo, O. M. Aluko and S. Umukoro (2018). Psychopharmacological evaluation of antidepressantlike activity of ethanol seed extract of grains of paradise (*Aframomum melegueta* K. Schum.) in mice, J. Food Biochem. 42, e12528. DOI: 10.1111/jfbc.12528
- [94] H. Hattori, T. Mori, T. Shibata, M. Kita and T. Mitsunaga (2021). 6-Paradol acts as a potential antiobesity vanilloid from grains of Paradise, *Mol. Nutr. Food Res.* 65, 2100185. DOI: 10.1002/mnfr.202100185
- [95] K. T. Biobaku, O. M. Azeez, S. A. Amid, T. N. Asogwa, A. A. Abdullahi, O. L. Raji and J. A. Abdulhamid (2020). Thirty days oral *Aframomum melegueta* extract elicited analgesic effect but influenced cytochrome p4501BI, cardiac troponin T, testicular alfa-fetoprotein and other biomarkers in rats, *J. Ethnopharmacol.* 267, 113493. DOI: 10.1016/j.jep.2020.113493
- [96] A. F. Goumtsa, F. Nokam, C. W. Koho, C. M. M. Dial and T. B. Nguelefack (2025). Antihypertrophic effects of the seed ethanolic extract of *Aframomum pruinosum* Gagnep. (Zingiberaceae) against isoproterenol-induced cardiac hypertrophy in male wistar rat, *Toxicol. Rep.* 14, 101855. DOI: 10.1016/j.toxrep.2024.101855
- [97] L. López-Ríos, M. A. Barber, J. Wiebe, R. P. Machín, T. Vega-Morales and R. Chirino (2021). Influence of a new botanical combination on quality of life in menopausal Spanish women: results of a randomized, placebo-controlled pilot study, *PLoS One* 16, e0255015. DOI: 10.1371/journal.pone.0255015
- [98] U. Inegbenebor, M. I. Ebomoyi, K. A. Onyia, K. Amadi and A. E. Aigbiremolen (2010). Effect of alligator pepper (Zingiberaceae *Aframomum melegueta*) on first trimester pregnancy in Sprague Dawley Rats, *Niger. J. Physiol. Sci.* 24, 161-164.

- [99] M. Bonnet-Duquennoy, M. Dumas, A. Debacker, K. Lazou, S. Talbourdet, J. Franchi, C. Heusèle, P. André, S. Schnebert, F. Bonté and R. Kurfürst (2007). Transcriptional effect of an *Aframomum angustifolium* seed extract on human cutaneous cells using low-density DNA chips, *J. Cosmet. Dermatol.* 6, 128-134.
- [100] P. O. Ottu, C. Oluwamodupe, A.F. Oluwatobiloba, I. O. Kehinde, O. A. Akinola, S. O. Ibrahim and O. O. Elekofehinti ((2025). Investigation of *Aframomum melegueta* compounds as ERK5 inhibitor related to breast cancer via molecular docking and dynamic simulation, *In. Silico. Pharmacol.* 13, 18. DOI: 10.1007/s40203-025-00304-w
- [101] R. Pérez-Machín, C. Elvira-Aranda, L. Lledó-Rico, M. J. Gomis-Gomis and L. López-Ríos (2025). *Aframomum melegueta* seed extract's effects on anxiety, stress, mood, and sleep: a randomized, doubleblind, pilot clinical trial, *Pharmaceuticals (Basel)* 18, 278. DOI: 10.3390/ph18020278
- [102] B. O. Ejechi, A. Ojeata and S. B. Oyeleke (1997). The effect of extracts of some Nigerian spices on biodeterioration of Okro (Abelmoschus (L) Moench) by Fungi, J. Phytopathol. 145, 469-472.
- [103] B. M. Okeke, S. A. Adefegha, S. I. Oyeleye and G. Oboh (2018). Effects of combined crude alkaloidrich extracts from alligator pepper (*Aframomum melegueta*) and bastered melegueta (*Aframomum danielli*) on the enzymes crucial to erectile dysfunction-in vitro, *J. Food Biochem.* 42, e12550. DOI: 10.1111/jfbc.12550
- [104] S. Eyob, A. Tsegaye and M. Appelgren (2008). Analysis of korarima (*Aframomum corrorima* (Braun) P.C.M. Jansen) indigenous production practices and farm based biodiversity in southern Ethiopia, *Genet. Resour. Crop Ev.* 56, 573-585.
- [105] G. Adegoke, R. Gbadamosi, F. Evwoerhurhoma, P. Uzo-peters, K. Falade, O. Itiola, O. Moody and B. Skura (2002). Protection of maize (Zea mays) and soybeans (Glycine max) using *Aframomum danielli*, *Eur. Food Res. Technol.* 214, 408-411.

