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REVIEW ARTICLE

# Botanical description, ethnomedicinal uses, phytochemistry, and pharmacological activities of genus *Kniphofia* and *Aloe:* A review

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**KEYWORDS**

*Kniphofia*;
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**Abstract** Genus *Kniphofia* and *Aloe* belong to Asphodeloideae and Alooideae subfamily of Asphodelaceae respectively. Asphodelaceae is a family of lily-related monocotyledonic flowering plants with 2 subfamilies, 16 genera and about 780 species distributed in arid and mesic regions of the temperate, subtropical and tropical zones of the old world, with the main center of diversity in southern Africa. The genus *Kniphofia* has about 70 species distributed in eastern and southern Africa, including the 7 species known to occur in Ethiopia, of which 5 species are endemic. *Aloe* is the largest genus among the Asphodelaceae family and it comprises of more than 400 species that are widely distributed in Africa, India, and other arid areas, with the major diversity in South Africa. The leaves of *Kniphofia* species are non-succulent, unlike the leaves of *Aloe* species. *Aloe* species are distinguished by having fleshy and cuticularized leaves usually with spiny margins. *Kniphofia* species have regular flowers with fused tepals while *Aloe* species have regular flowers with free tepals. Both *Kniphofia* and *Aloe* species have been employed in ethnopharmacology and have provided many bioactive compounds through phytochemical-pharmacological research works. They are traditionally used for treatment of various diseases by herbalists. Both genus elaborate naphthoquinone, pre-anthraquinone, anthraquinones and alkaloids in common. Additionally, *Kniphofia* elaborates benzene, naphthalene, and phloroglucinol derivatives while *Aloe* produces anthrones and chromones. The genus *Kniphofia* is rich in Knipholone type compounds while the genus *Aloe* is rich in anthrone-C-glycosides. Secondary metabolites isolated from the two genus have wide range of pharmacological activities such as antiplasmodial, anticancer, anti-inflammatory, antioxidant and antimicrobial activities. There is no published review article on the botanical description, traditional

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uses, phytochemistry, and pharmacological activities of the genus *Kniphofia* and only few review articles are available on the genus *Aloe*. In this review, an attempt is made to present pharmacological activities and secondary metabolites reported to date from genus *Kniphofia* and *Aloe*. Secondary metabolites reported from both plant genus have interesting biological activities so the authors of this review paper strongly recommend studies on toxicity of these compounds and their structural activity relationship so as to develop new pharmaceutical drug.



## 1. Introduction

Genus *Kniphofia* and *Aloe* belong to the subfamily Asphodeloideae and Alooideae of the family Asphodelaceae respectively (Bringmann et al., 2008). Asphodelaceae is a family of lily-related monocotyledonic flowering plants with 2 subfamilies, 16 genera and about 780 species distributed in arid and mesic regions of the temperate, subtropical and tropical zones of the old world, with the main center of diversity in southern Africa (Bringmann et al., 2008; Demissew & Nordal, 2010; Smith, 1998). In addition to *Kniphofia*, Asphodeloideae subfamily consists of *Asphodeline, Asphodelus, Bulbine, Bulbinella, Eremurus, Jodrellia, Simethis,* and *Trachyandra while* Alooideae subfamily comprises *Astroloba, Chamaealoe, Gasteria, Haworthia, Lomatophyllum,* and *Poellnitzia* in addition to *Aloe* (Bringmann et al., 2008). Asphodelaceae plants have leaves arranged in a basal rosette and regular flowers with fused tepals (in *Kniphofia*) or free tepals (in all other genera), which may be white, greenish, yellow, pink or red (Demissew & Nordal, 2010; Edwards et al.,1997).

Both *Kniphofia* and *Aloe* species have been employed in ethnopharmacology and have provided many bioactive compounds through phytochemical-pharmacological research works (Table 2-5). Species of genus *Kniphofia* have been traditionally used to treat a variety of ailments in different African countries (Table 2). *Kniphofia* species primarily elaborate anthraquinones, as well as other compounds including benzene, naphthalene, and phloroglucinol derivatives, and alkaloids with wide range of pharmacological activities (Sema et al., 2018). On the other hand, plants of the genus *Aloe* have been used medicinally to cure different diseases in Africa, Asia, Europe and the Middle East for hundreds of years and they are included in many commercial preparations for various applications (Belayneh et al., 2020). *Aloe* species are the rich natural sources of bioactive compounds; majority of them being anthraquinones (Puia et al., 2021). There is no published review article on the botanical description, traditional uses, phytochemistry, and pharmacological activities of the genus *Kniphofia* and only few review articles are available on the genus *Aloe*. Therefore, the aim of this review is to compile reports on the botanical description, ethnomedicinal uses, phytochemistry and pharmacological activities of the genus *Kniphofia* and *Aloe*.

## 2. The review methodology

### 2.1. The study design

In this study, a comprehensive review design was used to compile information on the botanical descriptions, ethnomedicinal uses, phytochemistry and pharmacological properties of genus *Kniphofia* and *Aloe*.

### 2.2. The search strategy

The relevant sources were retrieved by using search engines such as Google Scholar and PubMed. Specific keywords, phrases and synonyms such as *Kniphofia*/genus *Kniphofia*/*Kniphofia species*/*Kniphofia* plants, *Aloe*/genus *Aloe*/*Aloe species*/*Aloe* plants, botanical descriptions/informations, ethnomedicinal uses/values or traditional uses/values or ethnopharmacological uses/-values, phytochemistry or phytochemicals or secondary metabolites or natural products or compounds, pharmacological properties/activities or biological properties/activities were used for searching available literatures for the review.

### 2.3. Inclusion and exclusion criteria

Studies reporting botanical descriptions and/or ethnomedicinal uses of genus or specific species of *Kniphofia* and/or *Aloe* were included while reports on other related genus in the family Asphodelaceae were excluded in this review. Concerning phytochemistry part, studies reporting pure compounds isolated from the two genus and structurally characterized by spectroscopic techniques were included. However, those articles focusing only on qualitative analysis such as phytochemical screening tests or detection of compounds in the crude extract by using GC–MS or HPLC techniques and quantitative determinations of phytochemicals such as total phenol, total flavonoid, etc. were excluded. Regarding pharmacological properties, both *in vitro* and/or *in vivo* studies conducted on the crude extracts and/or isolated compounds were included while reports on biological activities of other derivatives such as nanoparticles synthesized from crude extracts and/or isolated compounds were excluded. In all cases, studies published in languages other than English were also excluded in this review.

### 2.4. Study selection

After collecting all sources, selection was made by quick analysis of the topics, abstracts and conclusions of the retrieved sources for eligibility criteria. Then after, the selected sources were deeply analyzed for preparation of this review article.

### 2.5. Softwares used

ChemDraw Ultra 8.0 software was used to draw the chemical structures of compounds and Mendeley Desktop reference management software was used to provide citations and references in this review.

**Table 1** Reynold's Grouping of Tropical African *Aloes*.

| Group | Description | Representative species | References |
|---|---|---|---|
| **Group 1** | Grass *Aloes*: Long and narrow leaves that have a grass like appearance | *A. myriacontha* | (Ayana, 2015) |
| **Group 2** | Lepto *Aloes*: Short-stemmed | *A.nuttii* | (Ayana, 2015) |
| **Group 3** | Bulbous species | *A. bkettneri* | (Ayana, 2015) |
| **Group 4** | Perianth striped | *A. peckii, A. rugosifolia, A. pirottae* | (Dagne et al., 1994) |
| **Group 5** | Compact rosettes or larger with open rosettes | *A. dorotheae* | (Dagneet al., 1994) |
| **Group 6** | Sapanariae: Plants with perianth pronounced basal inflation | *A. lateritia, A. dumetorum, A. graminicola* | (Dagne et al., 1994) |
| **Group 7** | Hereroenses: Plant sacaulescent or short-stemmed | *A. hereroensis* | (Ayana, 2015) |
| **Group 8** | Perianth trigonously indented above the ovary | *A. chabaudii, A. rivae* | (Dagne et al., 1994) |
| **Group 9** | Verae: Plants acaulous rarely caulescent, solitary or in group | *A. barbadensis, A. pubescens* | (Dagne et al., 1994) |
| **Group 10** | Pendet series | *A. veseyi* | (Ayana, 2015) |
| **Group 11** | Later bracteatae: Plants with bracts large, broadly ovate or suborbicular | *A. cryptopoda* | (Demissew & Nordal, 2010) |
| **Group 12** | Acaulescent or short stemmed | *A. christianii* | (Ayana, 2015) |
| **Group 13** | Perianths clavate | *A. camperi, A. calidophila, A. sinana* | (Dagne et al., 1994) |
| **Group 14** | Orthologhae: Flowers secund | *A. secundiflora, A. ortholopha* | (Dagne et al., 1994) |
| **Group 15** | Racemes bottle brush like: Plants with racemes densely flowered | *A. aculeate* | (Ayana, 2015) |
| **Group 16** | Large compact rosettes | *A. percrassa, A. harlana* | (Dagne et al., 1994) |
| **Group 17** | Leaves spreading, canaliculated | *A. magalacantha, A. schelpei* | (Dagne et al., 1994) |
| **Group 18** | Tall stemmed species | *A. volkensii* | (Ayana, 2015) |
| **Group 19** | Shrubs | *A. dawei, A. arborescens* | (Dagne et al., 1994) |
| **Group 20** | Trees | *A. eminens* | (Ayana, 2015) |

## 3. Botanical description of genus *Kniphofia* and *Aloe*

### 3.1. Botanical description of genus *Kniphofia*

The genus *Kniphofia* named after the German botanist Johann Hieronymus Kniphof belongs to the subfamily Asphodeloidea of the family Asphodelaceae (Gebru, 2010). The genus includes about 70 species distributed essentially in eastern and southern Africa, including the 7 species known to occur in Ethiopia, of which 5 species are endemic (Demissew & Nordal, 2010). Plants of this genus grow from a thick rhizome in aggregates or solitarily, rarely with a thick, well developed woody stem. The leaves are arranged in basal rosettes, usually in 4 or 5 ranks, linear, tapering gradually to the apex (Demissew & Nordal, 2010). The leaves of *Kniphofia* species are non-succulent, unlike the leaves of *Aloe* species (Bringmann et al., 2008) and the flowers are usually pendulous, with varied colors: white, yellow, brownish or red (Demissew & Nordal, 2010). The flowering season is either winter or summer depending on the species (Bringmann et al., 2008). Most *Kniphofia* species grow near rivers or in damp or marshy areas although few species prefer dry conditions with good drainage (Bringmann et al., 2008).

### 3.2. Botanical description of genus Aloe

*Aloe* is the largest genus among the Asphodelaceae family and it comprises of more than 400 species ranging from diminutive shrubs to large trees that are widely distributed in Africa, India, and other arid areas, with the major diversity in South Africa. *Aloe* is represented in East Africa by 83 species, of which 38 grow naturally in Ethiopia, including 15 endemic species (Abdissa et al., 2017). They are distinguished by having fleshy and cuticularized leaves usually with spiny margins. Its name is taken from the Arabic word "Alloeh", meaning "shining bitter substance" (Surjushe et al., 2008). There are 20 different groups (group 1 to 20) of the species of these plants according to Reynolds division by their similarities in morphology as depicted in Table 1.

## 4. Ethnomedicinal uses of genus *Kniphofia* and *Aloe*

### 4.1. Ethnomedicinal uses of genus *Kniphofia*

Genus *Kniphofia* has many records of medicinal values in treatment of various diseases. Its uses in treatment of hepatitis B, abdominal cramps, wound, gonorrhea and eradicating

**Table 2** Ethnomedicinal uses of *Kniphofia* species.

| Plant species | Part used | Disease treated | References |
|---|---|---|---|
| *K. foliosa* | Leaves | Hepatitis | (Yineger et al., 2007) |
| | Roots | Abdominal cramps and wound | (Dagne & Steglich, 1984; Wube et al., 2006;Wube et al., 2005) |
| | Not specified | Endoparasites of cattle | (Schmelzer et al., 2008) |
| *K. isoetifolia* | Roots | Gonorrhea and hepatitis B | (Yineger et al., 2008) |
| | Not specified | Wound | (Meshesha et al., 2017) |
| *K. caulescens* | Root bulb | Headache, eye pain and fatigue | (Mugomeri et al., 2016) |
| *K. northiae* | Stems | Prolonged periods in women, and related pains | (Mugomeri et al., 2016) |
| *K. drepanophylla* | Rhizomes | Ringworm, wounds, pimples, acne, and eczema | (Sagbo & Mbeng, 2018) |
| | Root | Tuberculosis | |
| *K. reflexa* | Rhizomes | High relapsing fever | (Sema et al., 2018) |
| *K. crassifolia* | Rhizomes | Orchitis | (Ramarumo et al., 2019) |
| | Rhizomes Flower | Hydrocele<br>Varicocele | |
| | Whole part | Erectile dysfunction | |
| *K. sumarae* | Leaves and flowers | Malaria | (Mothana et al., 2009) |
| *K. buchananii*<br>*K. parviflora*<br>*K. laxiflora*<br>*K. rooperi* | Not specified | Snake bite and chest ailments | (Bringmann et al., 2008) |
| *K. linearifolia* | Root | Infertility of women | (Schmelzer et al., 2008) |

**Table 3** Ethnomedicinal uses of *Aloe species*.

| Plant species | Part used | Disease treated | References |
|---|---|---|---|
| *A. macrocarpa* | Root Latex Fresh leaf | Impotency in men, Malaria, Bloat and fire burn | (Chekole et al., 2015; Bula & Baressa, 2017) |
| *A. trichosantha* | Latex | Malaria, Stomach ache, Gonorrhea, Impotency in men | (Bula & Baressa, 2017) |
| *A. citrina* | Latex | Swollen foot | |
| *A. monticola* | Root | Liver disease, Anthrax | (Abera, 2014; Bula & Baressa, 2017) |
| *A. gilbertii* | Leaves gel, roots and exudates | Malaria, Wounds | (Dessalegn, 2013) |
| *A. lateritia* | Exudates | Eye ailments | |
| *A. pulcherrima* | Sap | Asthma, Psychiatric disease | (Zenebe et al., 2012) |
| *A. kefaensis* | Latex | Fire burn | (Ayana, 2014) |

endoparasites of cattle are among the reported traditional uses of this genus in Ethiopia (Wube et al., 2006; Wube et al., 2005; Schmelzer et al., 2008; Dagne & Steglich, 1984; Meshesha et al., 2017; Yineger et al., 2007; Yineger et al., 2008). In other African countries, it is used in treatment of pain, prolonged periods in women, skin infections, tuberculosis, fever, infertility and as snake deterrent (Schmelzer et al., 2008; Bringmann et al., 2008; Ramarumo et al., 2019; Mothana et al., 2009; Mugomeri et al., 2016; Sagbo & Mbeng, 2018; Sema et al., 2018). Different parts of thLe plants such as leaves, roots, root bulb, stems, rhizomes and flowers are used in treatment of many ailments in traditional practices. Table 2 describes ethnomedicinal uses of genus *Kniphofia*.

### 4.2. Ethnomedicinal uses of genus Aloe

*Aloe* species have played important role in medicinal and economic history since 1500 BCE and the gel found in the interior of their leaves has been used to cure human and animals diseases (Abdissa et al., 2017). Plants in genus *Aloe* have been used for a broad range of medicinal purposes by traditional healers from wide variety of cultural groupings in Africa (Dagne, 1996). As well as these plants have been visited by traditional healers to treat various diseases in Ethiopia as depicted in Table 3. In rural parts of the country, its mucilaginous fluid applied to cuts and wounds in order to prevent infections and bring about healing (Tadesse & Mesfin, 2010).

**Table 4** Secondary metabolites reported from *Kniphofia* species.

| Compounds | Species (part) | Reference |
|---|---|---|
| **Naphthoquinone** | | |
| 3,5,8-trihydroxy-2-methylnaphthalen-1,4-dione (**1**) | *K. isoetifolia* (roots) | (Meshesha et al., 2017) |
| **Pre-anthraquinones** | | |
| Aloesaponol III (**2**) | *K. foliosa* (stem) | (Yenesew et al., 1994) |
| Aloesaponol III-8-methyl ether (**3**) | | |
| **Monomeric anthraquinones** | | |
| Chrysophanol (**4**) | *K. foliosa* (rhizomes) | (Gebru, 2010) |
| | *K. isoetifolia* (roots) | (Meshesha et al., 2017) |
| | *K. foliosa* (roots) | (Dagne & Steglich, 1984; (Wube et al., 2005) |
| | *K. foliosa* (leaves) | (Berhanu & Dagne,1984) |
| | *K. thomsonii* (roots) | (Achieng, 2009) |
| | *K. ensifolia* (whole part) | (Dai et al., 2014) |
| | *K. reflexa* (rhizomes) | (Sema et al., 2018) |
| Islandicin (**5**) | *K. foliosa* (rhizomes) | (Gebru, 2010) |
| | *K. thomsonii* (roots) | (Achieng, 2009) |
| Laccaic acid D (**6**) | *K. foliosa* (rhizomes) | (Gebru, 2010) |
| Aloe-emodin acetate (7) | *K. foliosa* (leaves) | (Berhanu & Dagne,1984) |
| | *K. thomsonii* (roots) | (Achieng, 2009) |
| Aloe-emodin (**8**) | *K. thomsonii* (roots) | (Achieng, 2009) |
| | *K. ensifolia* (whole part) | (Dai et al., 2014) |
| Physcion (**9**) | *K. thomsonii* (roots) | (Achieng, 2009) |
| Kniphofione A (**10**) | *K. ensifolia* (whole part) | (Dai et al., 2014) |
| Kniphofione B (**11**) | | |
| **Dimeric anthraquinones** | | |
| Asphodeline (**12**) | *K. isoetifolia* (roots) | (Meshesha et al., 2017) |
| | *K. ensifolia* | (Dai et al., 2014) |
| 10-hydroxy-10-(chrysophanol-7′-yl) | *K. isoetifolia* (roots) | (Meshesha et al., 2017) |
| chrysophanolanthrone (**13**) | *K. foliosa* (roots) | (Wube et al., 2005) |
| | *K. ensifolia* | (Dai et al., 2014) |
| | *K. thomsonii* (roots) | (Achieng, 2009) |
| Chryslandicin (**14**) | *K. foliosa* (roots) | (Wube et al., 2005) |
| | *K. ensifolia* | (Dai et al., 2014) |
| | *K. thomsonii* (roots) | (Achieng, 2009) |
| 10, 10′-bichrysophanol anthrone (**15**) | *K. thomsonii* (roots) | (Achieng, 2009) |
| 10-hydroxy-10-(chrysophanol-7′-yl)-aloe-emodinanthrone (**16**) | | |
| 10-hydroxy-10-(islandicin-7′-yl)-aloe emodin anthrone (**17**) | | |
| Microcarpin (**18**) | *K. ensifolia* | (Dai et al., 2014) |
| 10-methoxy-10,7′-(chrysophanol anthrone)-chrysophanol (**19**) | *K. foliosa* (roots) | (Abdissa et al., 2013) |
| **Phenyl anthraquinones** | | |
| Knipholone (**20**) | *K. foliosa* (rhizomes) | (Gebru, 2010) |
| | *K. foliosa* (roots) | (Dagne & Steglich, 1984; (Wube et al., 2005) |
| | *K. foliosa* (leaves) | (Berhanu & Dagne,1984) |
| | *K. thomsonii* (roots) | (Achieng, 2009) |
| | *K. reflexa* (rhizomes) | (Sema et al., 2018) |
| | *K. ensifolia* | (Dai et al., 2014) |
| Knipholone anthrone (**21**) | *K. foliosa* (stem) | (Dagne &Yenesew,1993) |
| Isoknipholone (**22**) | *K. foliosa* (stem) | (Yenesew et al., 1994) |
| Isoknipholone anthrone (**23**) | | |
| Foliosone (**24**) | | |
| Isofoliosone (**25**) | | |
| Knipholone cyclooxanthrone (**26**) | *K. foliosa* (roots) | (Abdissa et al., 2013) |
| 10-acetonylknipholone cyclooxanthrone (**27**) | *K. foliosa* (rhizomes) | (Induli et al., 2013) |
| **Dimeric phenyl anthraquinones** | | |
| Joziknipholone A (**28**) | *K. foliosa* (rhizomes) | (Gebru, 2010; Induli et al., 2013) |
| JoziknipholoneB (**29**) | | |
| **Tetrameric phenyl anthraquinone** | | |
| Jozi-joziknipholone anthrone (**30**) | *K. foliosa* (rhizomes) | (Gebru, 2010) |

(*continued on next page*)

**Table 4** (*continued*)

| Compounds | Species (part) | Reference |
|---|---|---|
| **Other Compounds** | | |
| 3,4-dihydroxybenzoic acid (**31**) | *K. foliosa* (rhizomes) | (Gebru, 2010) |
| | *K. reflexa* (rhizomes) | (Sema et al., 2018) |
| 2-acetyl-1-hydroxy-8-methoxy- 3-methyl naphthalene (**32**) | *K. foliosa* (roots) | (Wube et al., 2005) |
| | *K. reflexa* (rhizomes) | (Sema et al., 2018) |
| 4,6-dihydroxy-2-methoxyacetophenone (**33**) | *K. foliosa* (stem) | (Yenesew et al., 1994) |
| Flavoglaucin (**34**) | *K. thomsonii* (roots) | (Achieng, 2009) |
| 3′'',4′''-dehydroflavoglaucin (**35**) | | |
| Kniphofiarindane (**36**) | *K. reflexa* (rhizomes) | (Sema et al., 2018) |
| Kniphofiarexine (**37**) | | |
| Dianellin (**38**) | *K. foliosa* (roots) | (Abdissa et al., 2013) |
| N,N,N'-trimethyl-N'-[4-hydroxy-*cis*-cinnamoyl]-putrescin (**39**) | *K. foliosa*, *K. flavovirens, K. tuckii* (leaves) | (Ripperger et al., 1970) |
| N,N,N'-trimethyl-N'-[4-methoxy-*cis*-cinnamoyl]-putrescin (**40**) | | |

**Table 5** Secondary metabolites reported from *Aloe* species.

| **Compounds** | **Species (part)** | **Reference** |
|---|---|---|
| **Alkaloids** | | |
| Coniine (**41**) | *A. sabaea* (leaves) | (Blitzke et al., 2000) |
| Conhydrine (**42**) | *A. gillilandii* (leaves) | (Hotti & Rischer,2017) |
| g-Coniceine (**43**) | *A. krapholiana* (leaves) | (Dagne et al., 2000) |
| **Anthraquinones** | | |
| Chrysophanol (**4**), Helminthosporin (**44**), Aloeemodin (**8**), Aloesaponarin II (**45**), Aloesaponarin I (**46**) | *A. megalacantha* (root) | (Abdissa et al., 2017) |
| **Pre-anthraquinones** | | |
| Aloesaponol I (**47**) | *A. megalacantha* (root) | (Van Heerden et al., 2000) |
| Aloesaponol III (**2**), Aloesaponol IV (**48**), Aloesaponol-I-6-O-glucopyranoside(**49**), Aloesaponol-II-6-O-glucopyranoside (**50**), Aloesaponol-III-8-O-glucopyranoside (**51**) | *A. saponaria* (subterranean parts) | (Ayana, 2015) |
| **Anthrones** | | |
| Aloin A (**52**), Aloin B (**53**) | *A. castanea* (leaves exudate) | (Van Heerden et al., 2000) |
| 5-Hydroxyaloin A (**54**), AloinosideA (**55**), Aloinoside B (**56**) | *A. ferox* (leaf exudate) | (Adhami & Viljoen, 2015) |
| 10-hydroxyaloin B (**57**), Deacetyllittoraloin (**58**) | *A. littoralis* (leaf exudate) | (Karagianis et al., 2003) |
| **Naphthoquinones** | | |
| 6-hydroxy-3,5-dimethoxy-2-methyl-1,4-naphthoquinone (**59**), Ancistroquinone C (**60**), 5,8-dihydroxy-3-methoxy-2-methyl-1,4- naphthoquinone (**61**), Malvone A (**62**), Droserone (**63**), Droserone-5-methyl ether (**64**), Hydroxydroserone (**65**) | *A. dawei* (root) | (Abdissa et al., 2014)) |
| **Chromones** | | |
| 8-C-glucosyl-(S)-*O*-aloesol (**66**), 8-C-glucosyl-7-*O*-methylaloediol (**67**), 8-C-glucosyl noreugenin (**68**) | *A. vera* (leaves) | (Okamura et al., 1998) |
| Aloesin (**69**) | *A. monticola* (leaf latex) | (Hiruy et al., 2019) |
| 7-hydroxy-2,5-dimethyl- chromone (**70**), Furoaloesone (**71**), 2-acetonyl-8-(2-furoylmethyl)-7-hydroxy-5-methylchromone (**72**) | *A. ferox* (leaf exudates) | (Kametani et al., 2007) |
| 7-*O*-methyl-6-*O*-coumaroylaloesin (**73**) | *A. monticola* (leaf latex) | (Hiruy et al., 2019) |

## 5. Phytochemistry of genus *Kniphofia and Aloe*

### *5.1. Phytochemistry of genus* **Kniphofia**

The genus *Kniphofia* is a rich source of anthraquinones besides other compounds such as benzene, naphthalene and phloroglucinol derivatives as well as alkaloids (Sema et al., 2018). This genus is well known to elaborate mainly monomeric and dimeric anthraquinones as well as phenyl anthraquinones. Anthraquinones of genus *Kniphofia* have a common structural feature which is hydroxylation at C-1 and C-8 positions of the anthranoid nucleus. Methylation at C-3 position is also commonly observed in most anthraquinones of this genus. Sometimes, this methyl group can also be oxidized as in the case of compounds **7, 8, 10, 11, 16** and **17** (Fig. 1). The dimers of different types which are believed to be formed by inter or intramolecular oxidative coupling of monomeric anthraquinones through carbon-carbon bonds have also been reported commonly in this genus.

Genus *kniphofia* is also reported to be one of the three important sources of phenyl anthraquinones after the genera *Bulbine* and *Bulbinella* (Bringmann et al., 2008). This special class of anthraquinones have a phenyl group (acetyl phloroglucinol moiety) attached to a chrysophanol or chrysophanol anthrone at C-4 or C-10 positions. Phenyl anthraquinones of genus *kniphofia* can also exist in monomeric, dimeric and tetrameric forms. Phenyl anthraquinones in which the acetyl phloroglucinol moiety is linked to oxychrysophanol anthrone at C-10 (as in the case of compounds **24** and **25**) are called oxanthrones (Bringmann et al., 2008). Unusual monomeric

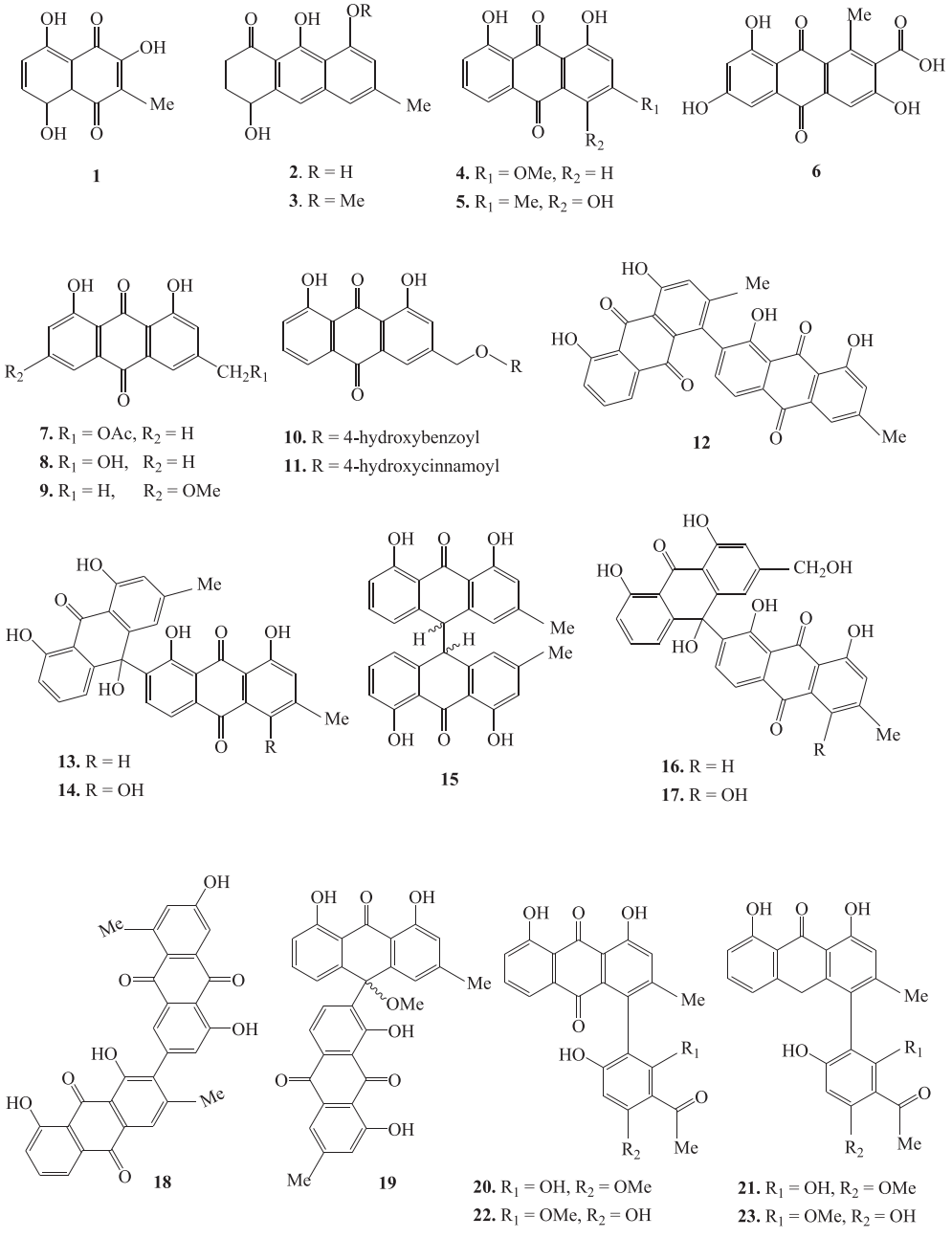


**Fig. 1** Chemical structures of secondary metabolites isolated from *Kniphofia species*.

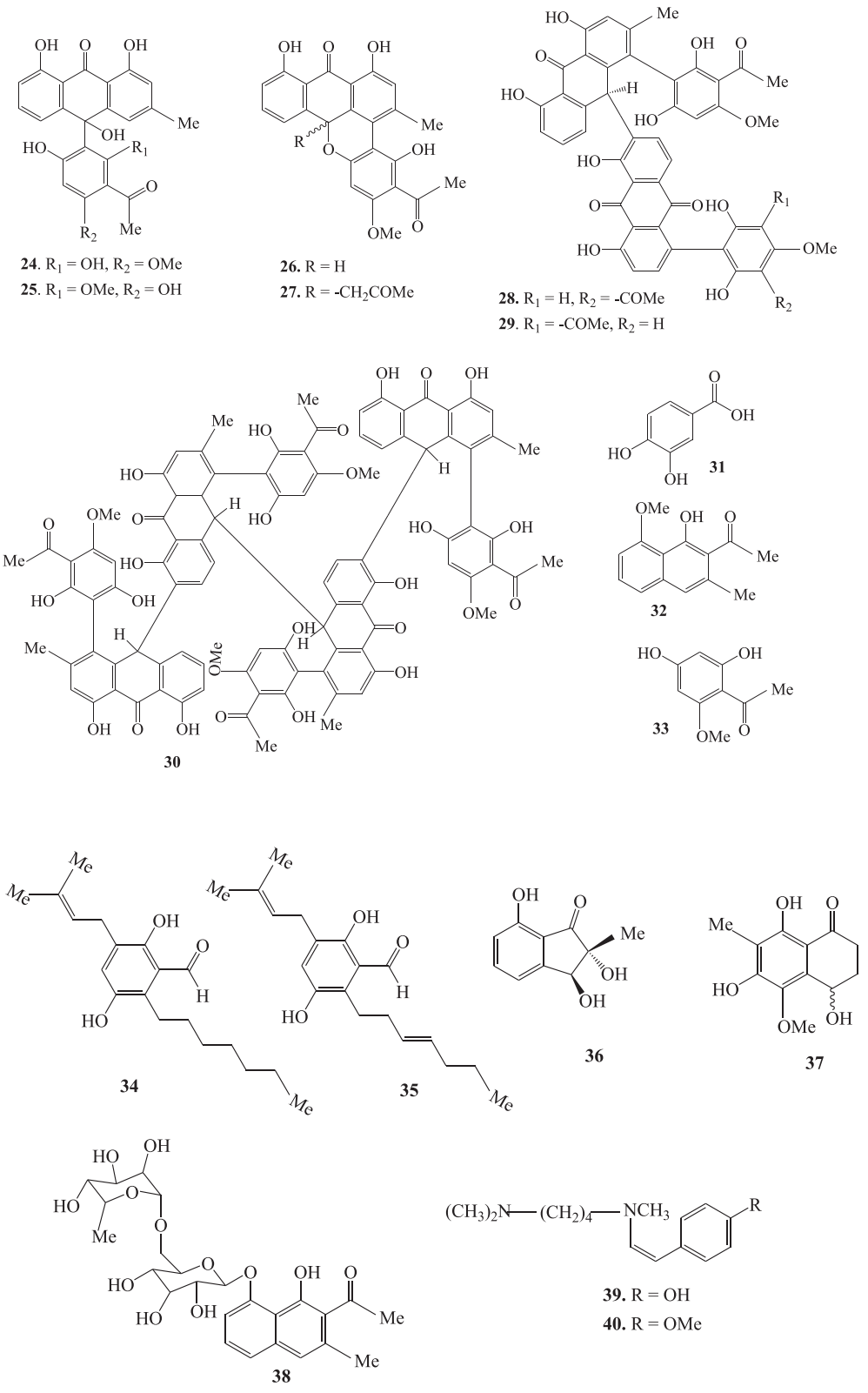


**Fig. 1** (*continued*)

phenyl anthraquinones in which cyclization involving C-10 and C-6′ via oxygen bridge leads to formation of one more ring (compounds **26** and **27**) have also been reported in this genus (N. Abdissa et al., 2013; Induli et al., 2013). Phenyl anthraquinones having acetyl phloroglucinol moiety coupled to chrysophanol or chrysophanol anthrone unit via C-4 like knipholone

(**20**) and its derivatives are by far the largest group in this genus (Bringmann et al., 2008). O-methylation pattern of the acetyl phloroglucinol moiety and/or the oxidation state of the anthranoid core leads to structural diversification among phenyl anthraquinones of this genus (Bringmann et al., 2008). Table 4 summarizes secondary metabolites isolated from different *Kniphofia* species.

### 5.2. Phytochemistry of genus Aloe

*Aloes* are interesting sources of various classes of secondary metabolites (Table 5 and Fig. 2). Regarding the different composition of leave portions of *Aloe* species, they are likely to have distinct classes of bioactive compounds; outer green epidermis has been reported to contain alkaloids, anthraquinones, pre-anthraquinones. While the outer pulp region below the epidermis contains latex that predominantly consists of phenolic compounds, including anthraquinones, pre-anthraquinones, anthrones, chromones, coumarins, and flavonoids (Salehi et al., 2018). Besides leaves and roots are also the site of storage for many interesting secondary metabolites such as anthraquinones, pre-anthraquinones, anthrones, chromones, and alkaloids (Koroch et al., 2009). Methylation at C-1 and hydroxylation at C-8 positions of the anthranoid unit is commonly observed in anthraquinones of genus *Aloe*. This genus is also rich in anthrone-C-glycosides.

## 6. Pharmacological activities of genus *Kniphofia and Aloe*

### 6.1. Pharmacological activities of genus **Kniphofia**

Anthraquinones which are the major secondary metabolites of Asphodelaceae family and genus *Kniphofia* have a wide range of pharmacological activities which include antiplasmodial, anticancer, anti-inflammatory, antioxidant and antimicrobial activities. The biological activities of genus *Kniphofia* are discussed in detail in the following sections.

#### 6.1.1. Antiplasmodial activities

10-methoxy-10, 7′-(chrysophanol anthrone)-chrysophanol (**19**), 10-acetonyl knipholone cyclo oxanthrone (**27**) and jozi-knipholone A (**28**) from *K. foliosa* were investigated for *in vitro* antiplasmodial activities against the chloroquine resistant (W2) and chloroquine sensitive (D6) strains of *Plasmodium falciparum* (Abdissa et al., 2013; Induli et al., 2013). Compound **19** showed good activity with $IC_{50}$ values of 1.17 ± 0.12 and 4.07 ± 1.54 μg/mL respectively. Compound **27** exhibited significant activity ($IC_{50}$ = 3.1 ± 1.2 μg/mL) against the W2 strain of *P. falciparum*. Compound **28** was found to be the most active compound with $IC_{50}$ values of 0.3 ± 0.1 μg/mL (against W2) and 0.4 ± 0.1 μg/mL (against D6).

10-(chrysophanol-7′-yl)-10 hydroxy chrysophanol anthrone (**13**) and chryslandicin (**14**) from the roots of *K. foliosa* were evaluated for their *in vitro* antimalarial activity against the chloroquine sensitive 3D7 strain of *P. falciparum* (Wube et al., 2005). Compounds **13** and **14** showed a high inhibition of the growth of *P. falciparum* with $ED_{50}$ values of 0.260 and 0.537 μg/mL, respectively. Compounds **13** and **14** were also isolated from *K. ensifolia* and reported to have strong antiplasmodial activities with $IC_{50}$ values of 0.4 ± 0.1 and 0.2 ± 0.1 μM, respectively against Dd2 strain of *P. falciparum* (Dai et al., 2014).

#### 6.1.2. Anticancer activities

The antiproliferative activity of the methanol extract of *K. sumarae* was tested *in vitro* against three human cancer cell lines; 5637, MCF-7, A-427 and showed an $IC_{50}$ values of greater than 50 μg/mL (Mothana et al., 2009). The cytotoxicity of knipholone (**20**) and knipholone anthrone (**21**) from *K. foliosa* was examined on leukaemic and melonocyte cancer cell lines (Habtemariam, 2010). Compound **21** was found to induce a rapid onset of cytotoxicity with $IC_{50}$ values ranging from 0.5 to 3.3 μM while compound **29** showed 70–480 times less cytotoxicity to cancer cells ($IC_{50}$-greater than 240 μM).

#### 6.1.3. Anti-inflammatory activities

Knipholone (**20**) and chrysophanol (**4**) from the rhizomes of *K. reflexa* showed moderate anti-inflammatory activity against ROS production with $CC_{50}$ value of 38.7 ± 4.90 and 20.00 ± 4.40 μg/mL, respectively (Sema et al., 2018). Compound **20** was also isolated from the roots of *K. foliosa* and investigated for inhibition of leukotriene biosynthesis in an *ex-vivo* bioassay using activated human neutrophile granulocytes (Wube et al., 2006). This compound was found to be a selective inhibitor of leukotriene metabolism in a human blood assay with an $IC_{50}$ value of 4.2 μM.

#### 6.1.4. Antioxidant activities

The free radical scavenging activity of methanol extract of *K. sumarae* was studied and reported to be 2.0, 6.8, 16.5, 66.1, 91.0 % at 10, 50, 100, 500 and 1000 μg/mL, respectively (Mothana et al., 2009). The antioxidant activity of knipholone (**20**) from the roots of *K. foliosa* was examined using various *in vitro* assay systems including free radical scavenging, non-enzymatic lipid peroxidation, and metal chelation (Wube et al., 2006). Knipholone was found to be a weak dose-independent free radical scavenger and lipid peroxidation inhibitor, but not a metal chelator. The radical scavenging activity of knipholone tested on the stable DPPH radical showed a very weak antioxidant property with an $IC_{50}$ value of 355 μM compared to the positive control, quercetin ($IC_{50}$ = 3.2 μM). Knipholone was also found to be a weak inhibitor of phospholipids liposomes peroxidation with an $IC_{50}$ value of 311 μM compared to the positive control, quercetin ($IC_{50}$ = 1.4 μM).

The antioxidant potential of knipholone anthrone (**21**) from *K. foliosa* was assessed using a variety of *in vitro* assay models (Habtemariam, 2007). This compound displayed $IC_{50}$ value of 22 ± 1.5 μM in the DPPH assay while the positive control, (-)-epicatechin showed $IC_{50}$ value of 8.7 ± 0.9 μM. The compound displayed a better activity than (-)-epicatechin in scavenging superoxide anions and preventing deoxyribose degradation by hydroxyl radicals. The compound was found to form a complex with iron (II) ion ($Fe^{2+}$), displaying a concentration-dependant reducing power and also protected (at concentration of greater than 4.4 μM) isolated DNA from damage induced by Fenton reaction-generated hydroxyl radicals.

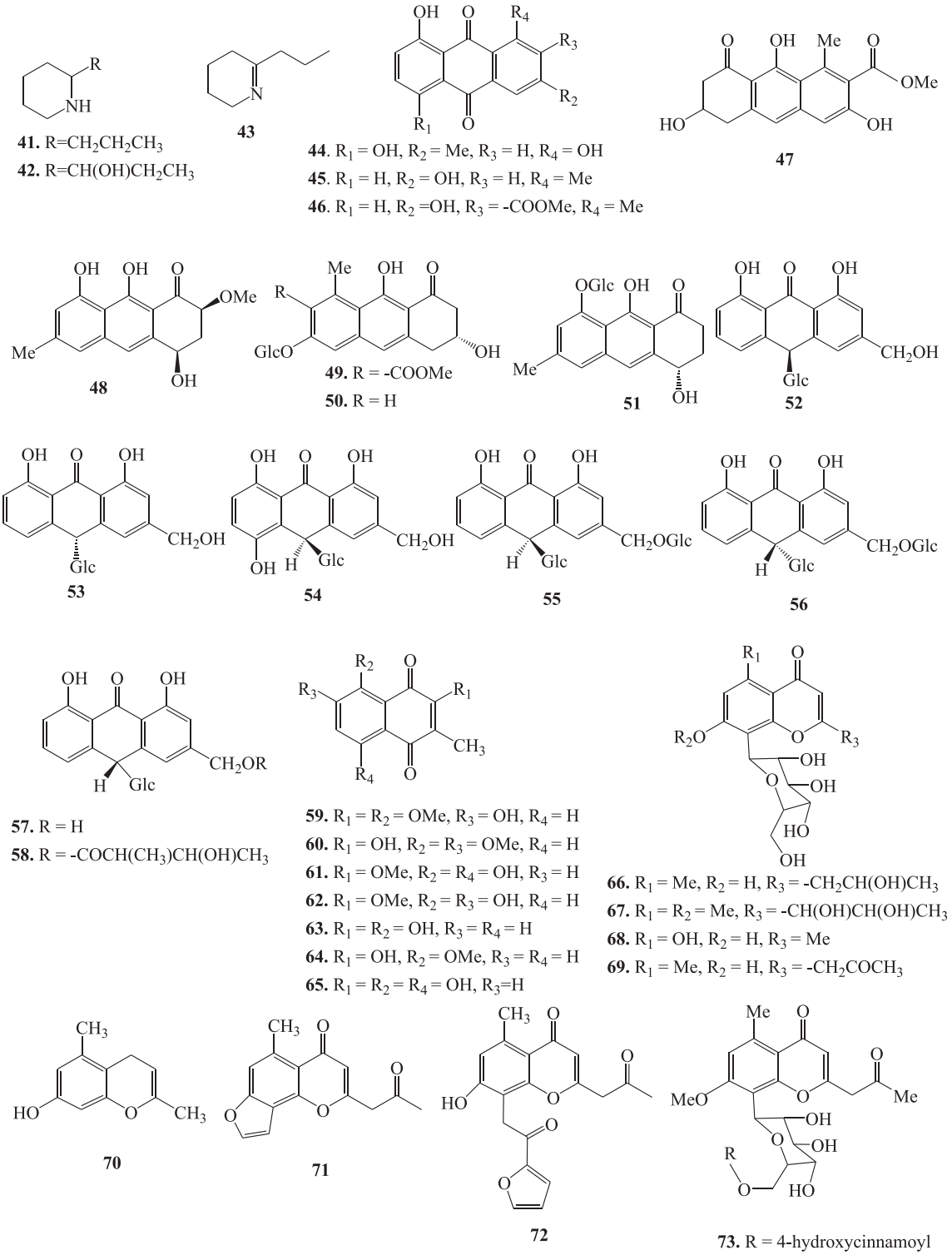


**Fig. 2** Chemical structures of secondary metabolites isolated from *Aloe species*.

*6.1.5. Antimicrobial activities*

The antimicrobial investigations of genus *Kniphofia* has been reported to be carried out against microorganisms including *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus flavus, Escherichia coli, Pseudomonas aeruginosa, Candida maltosa, Aliivibrio fischeri, Mycobacterium tuberculosis, Enterococcus faecalis, Klebsiella pneumonia, Salmonella typhimurium*.

The antimicrobial activity of methanol extract of *K. sumarae* was investigated against *S. aureus*, *B. subtilis*, *M. flavus, E. coli, P. aeruginosa* and *C. maltosa* (Mothana et al., 2009). The crude extract showed inhibition zones of 11, 7, and 14 mm respectively for the first three organisms but no activity was observed for the last three organisms.

Knipholone (**20**) and knipholone anthrone (**21**) from *K. foliosa* were tested for antibacterial activities against *A. fischeri* and *M. tuberculosis* (Feilcke et al., 2019). No more than 30% growth inhibition was observed at concentrations up to 100 μM and 10 μg/mL suggesting that both compounds have minimal antibacterial activities.

The $CHCl_3/CH_3OH$ (1:1) crude extract and pure compounds from the roots of *K. isoetifolia* were evaluated for *in vitro* antibacterial activity against *S. aureus, E. faecalis, P. aeruginosa* and *E. coli* (Meshesha et al., 2017). The crude extract showed inhibition zone of 23 ± 0.81, 23 ± 0.89, 22 ± 0.30 and 28 ± 0.51 mm respectively against the listed bacteria. The isolated compounds were also evaluated and the inhibition zone of 16 ± 0.15, 19 ± 0.15, 23 ± 0.06, 17 ± 0.06 for 3,5,8-trihydroxy-2-methylnaphthalene-1,4-dione (**1**), 10 ± 0.26, 18 ± 0.06, 17 ± 0.25, 16 ± 0.30 for chrysophanol (**4**), 22 ± 0.32, 30 ± 0.12, 22 ± 0.06, 20 ± 0.05 for asphodeline (**12**) and 25 ± 0.01, 28 ± 0.15, 17 ± 0.15, 18 ± 0.06 mm for 10-hydroxy-10,7 -(chrysophanol anthrone) chrysophanol (**13**) were recorded respectively against the mentioned organisms. Among the tested compounds, chrysophanol (**4**) was found to be the least active (10–18 mm) while asphodeline (**12**) demonstrated relatively good zone of inhibition (20–30 mm).

The *in vitro* antibacterial activity of acetone crude extract of *K. pumila* was investigated and it was found to show growth inhibition zone of 12.6 ± 0.39, 11.8 ± 0.41, 10.7 ± 0.32 and 9.7 ± 0.28 mm against *E. coli, K. pneumonia, S. aureus* and *S. typhimurium*, respectively (Abdissa et al., 2020). Knipholone (**20**), the compound isolated from this plant displayed better activity than the crude extract against *E. coli, S. aureus* and *S. typhimurium*, with inhibition zone of 14 ± 0.13, 16 ± 0.42 and 12 ± 0.13 respectively.

### 6.2. Pharmacological activities of genus *Aloe*

As various report showed, the genus *Aloe* has interesting biological activities including antimicrobial, antiplasmodial, antioxidant, anticancer, anti-inflammatory, and larvicidal activities.

#### 6.2.1. Antimicrobial activities

The antimicrobial investigations of genus *Aloe* has been reported to be conducted against microorganisms such as *Bacillus cereus, Escherichia coli, Pseudomonas aeruginosa, Candida albicans, Salmonella typhimurium, Aspergillus niger, Fusarium oxysporum,* and different viruses.

The antibacterial activity of the leaves of *A. rupestris* and *A. maculatavar* were evaluated *in vitro* against *B. cereus* and showed inhibition zone of 22.3 ± 1.52 and 21.0 ± 2.0 mm respectively (Sonam & Archana, 2015; Omer et al., 2017). The leaves latex of *A. monticola* was also determined for *in vitro* antibacterial activity against *S. typhi* and showed inhibition zone of 15.0 ± 0.6 (Waithaka et al., 2018). The antibacterial activity of the leaves of *A. vera* was assessed against *E. coli* and *P. aeruginosa* and found to have inhibition zone of 29 and 20 mm respectively (Abakar et al., 2017). *A. pulcherrima* roots was also evaluated against *P. aeruginosa* and revealed inhibition zone of 21 mm (Abdissa et al., 2017). The leaves of *A. vera* was evaluated for its antifungal activity and showed inhibition zone of 20 and 23 mm against *C. albicans* and *A. niger* respectively (Saniasiaya et al., 2017; Waithaka et al., 2018). Antifungal activity of *A. volkensii* leaves pulp was also reported to have inhibition zone of 21 ± 1 mm against *F. oxysporum* (Waithaka et al., 2018). The antimicrobial activity of the *Aloe* species may attribute to the presence of chromones, anthraquinones, and their derivatives. As the screening for their *in vitro* antimicrobial activity shows compounds such as chrysophanol (**4**), Aloe-emodin (**8**), Aloesin (**69**), and 7-*O*-methyl-6′ -*O*-coumaroylaloesin (**73**) are promising antimicrobial agents (Hiruy et al., 2019; Malmir, 2017).

As shown in many reports crude extract of from *A. vera* has antiviral activity on several types of virus (Haemorrhagic viral, Rhobda virus septicaemia, Herpes simplex virus type 1, Herpes simplex virus type 2, Varicella-Zoster virus, human immunodeficiency virus, Influenza virus, Polio virus, Cytomegalo virus, Human papilloma virus) including Corona virus SARS-CoV-1 (Mpiana et al., 2020). Such promising antiviral activity of this *Aloe* plant may attribute to the presence of anthraquinone derivatives, such as aloe-emodin (**8**) and chrysophanol (**4**) which have been reported to exhibit antiviral activity against influenza A virus with reducing virus-induced cytopathic effect and inhibiting replication of influenza A virus (Kumar, 2017). Extracts from flowers, flower-peduncles, leaves, and roots of *A. hijazensis* have also been evaluated for antiviral activities of against avian influenza virus type A (AI-H5N1), Newcastle disease virus (NDV), and egg-drop syndrome virus (EDSV). Extract of the flowers and leaves have showed higher activity than the extracts of other plant parts (Abd-Alla et al., 2012).

#### 6.2.2. Antiplasmodial activities

Antiplasmodial/antimalarial activity of both crude extract and isolated anthrones (Aloin A (**52**) and aloin B (**53**) from the leaf latex of *A. percrassa* was studied *in vivo* using Peter's 4-day suppressive test. After a four day treatment of *P. berghei* infected mice with the extract at doses of 100, 200 and 400 mg/kg/day, chemosuppression of 45.9%, 56.8% and 73.6% was observed respectively for each dose. Aloin A/B showed chemo-suppression of 36.8, 51.1, and 66.8 % (Geremedhin et al., 2014). Compounds isolated from the roots of *A. pulcherrima*; chrysophanol (**4**), aloesaponarin II (**45**) and aloesaponarin I (**46**), were evaluated for their *in vitro* antiplasmodial activity using malaria SYBR Green I-based *in vitro* assay against chloroquine resistant (W2) and chloroquine sensitive (D6) strains of *P. falciparum*. The isolates; chrysophanol (**4**) ($IC_{50}$ 21.05 ± 0.64), aloesaponarin II (**45**) ($IC_{50}$ 5.00 ± 0.36) and aloesaponarin I (**46**) ($IC_{50}$ 7.80 ± 1.11) showed considerable *in vitro* antiplasmodial activity against chloroquine-sensitive (D6) strain. Moreover these anthraquinones; chrysophanol (**4**) ($IC_{50}$ 36.09 ± 3.32), aloesaponarin II (**45**) ($IC_{50}$ 18.60 ± 7.10) and aloesaponarin I ($IC_{50}$ 20.13 ± 5.12) (**46**) have also showed significant antiplasmodial activity against chloroquine-resistant (W2) (Abdissa et al., 2017).

#### 6.2.3. Antioxidant activities

The antioxidant capacities of crude extract of *A. gilbertii* were evaluated by using reducing power determination method. The methanol, ethanol, and ethyl acetate root extracts of the plant showed good antioxidant activity with 244.5 ± 0.631, 241.5 ± 0.112, and 106 ± 1.05 mg of ascorbic acid per 10 mg dry weight of antioxidant in the reducing power, respectively

(Yadeta, 2019). The ethanol extracts of the peels of *A. vera* have also been reported to have high antioxidant activity with values of 2.43 mM ET/g MF (DPPH), 34.32 mM ET/g MF (ABTS), and 3.82 mM ET/g MF (FRAP).Total antioxidant activity was determined as the capturing of the DPPH and ABTS radicals, while the iron-reducing antioxidant power (FRAP) was analyzed by spectroscopic methods (Quispe et al., 2018).

#### *6.2.4. Anticancer activities*

Petroleum ether extract of *A. perryi* flowers was evaluated for its antiproliferative activity against seven human cancer cell lines (HepG2, HCT-116, MCF-7, A549, PC-3, HEp-2 and HeLa) using MTT assay. The percentage inhibition of the extract was reported to be 92.6%, 93.9%, 92%, 90.9%, 88.9%, 82% and 85.7% for HepG2, HCT-116, MCF-7, A-549, PC-3, HEp-2 and HeLa cells, respectively (Al-Oqail et al., 2016). The *in vitro* anticancer activity of compounds isolated from *A. turkanensis* was evaluated using MTT assay against the human extra hepatic bile duct carcinoma (TFK-1) and liver (HuH7) cancer cell lines. The anthraquinone aloe-emodin (**8**) and the naphthoquinone 5,8-dihydroxy-3-me thoxy-2-methylnaphthalene-1,4- dione (**61**) exhibited high inhibition against TFK-1 cell lines with $IC_{50}$ values of 6.0 and 15.0 μg/mL (in TFK-1 cells) and 31 and 20 μg/mL (in HuH7 cell line), respectively (Fozia, 2014).

#### *6.2.5. Anti-inflammatory activities*

The anti-inflammatory activity of aqueous extract of *A. barbadensis* was investigated in rats using formalin-induced hind paw oedema. The results of the anti-inflammatory study revealed that 25, 50 and 100 mg/kg of the extract significantly reduced the formalin-induced oedema at the beginning of 3 h (Egesie et al., 2011). The anti-inflammatory activity of aqueous extract *A. ferox* leaf was studied using carrageenan and formaldehyde-induced rat paw oedema. The extract exhibited potential anti-inflammatory activity (78.2 and 89.3% for carrageenan and formaldehyde-induced rat paw oedema, respectively) at the dose of 400 mg/kg (Mwale & Masika, 2010).

#### *6.2.6. Larvicidal activities*

The ethyl acetate soluble extract of *A. turkanensis* was reported to have high larvicidal activity against the common malaria vector, *Anopheles gambie,* where 100% mortality was achieved at a concentration of 0.2 mg/ml and it had an $LC_{50}$ of 0.11 mg/ml (Matasyoh et al., 2008). Crude extract of *A. vera* have been screened for its larvicidal activity against *Musca domestica*. Three instars larvae of housefly were treated with the different concentrations by dipping method for 24 and 48 hrs. The $LC_{50}$ values of *A. vera* extract were found to be 32.67, 36 and 38.67 ppm in 24 hrs; 24, 25.67 and 28.33 ppm in 48 hrs on 1st, 2nd and 3rd instars respectively (Jesikha, 2012).

## 7. Conclusion

Botanically, genus *Kniphofia* and *Aloe* shares the same family (Asphodelaceae) while they belong to different subfamilies (Asphodoledeae and Aloideae respectively). They prefer different habitat and have different physical appearance regarding leaf and flower anatomy. Ethnomedicinally, species of the two genus are used for curing numerous ailments by herbalists. Phytochemically, both genus elaborate naphthoquinone, preanthraquinone, anthraquinones and alkaloids in common. Additionally, *Kniphofia* elaborates benzene, naphthalene, and phloroglucinol derivatives while *Aloe* produces anthrones and chromones. The anthraquinones of the two genus have different structural features. Most anthraquinones of genus *Kniphofia* are characterized by hydroxylation at C-1 and C-8, as well as methylation at C-3 positions of the anthranoid nucleus. Sometimes, the methyl group at C-3 position oxidizes to form alcohol or ester group. In the case of the genus *Aloe*, methylation at C-1 and hydroxylation at C-8 positions of the anthranoid unit is commonly observed. The genus *Kniphofia* is rich in Knipholone type compounds while the genus *Aloe* is rich in anthrone-C-glycosides. Pharmacologically, secondary metabolites isolated from the two genus have wide range of activities such as antiplasmodial, anticancer, anti-inflammatory, antioxidant and antimicrobial activities.

## 8. Author Agreement

We accept the terms of Author Agreement on the Arabian Journal of Chemistry.

## 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.

## References

Abd-Alla, H.I., Abu-Gabal, N.S., Hassan, A.Z., El-Safty, M.M., Shalaby, N.M.M., 2012. Antiviral activity of *Aloe hijazensis* against some haemagglutinating viruses infection and its phytoconstituents. Arch. Pharmacal Res. 35 (8), 1347–1354. https://doi.org/10.1007/s12272-012-0804-5.

Abdissa, D., Geleta, G., Bacha, K., Abdissa, N., 2017. Phytochemical investigation of *Aloe pulcherrima* roots and evaluation for its antibacterial and antiplasmodial activities. PLoS ONE 12, (3). https://doi.org/10.1371/journal.pone.0173882 e0173882.

Abdissa, D., Faye, G., Fayera, M., Demissie, S., 2020. Extraction and isolation of compound from roots of *kniphofia pumila*, and its antibacterial activities in combination with zinc chloride. Walailak J. Sci. Technol. 17 (7), 631–638.

Abdissa, N., Induli, M., Akala, H.M., Heydenreich, M., Midiwo, J.O., Ndakala, A., Yenesew, A., 2013. Knipholone cyclooxanthrone and an anthraquinone dimer with antiplasmodial activities from the roots of *Kniphofia foliosa*. Phytochem. Lett. 6 (2), 241–245. https://doi.org/10.1016/j.phytol.2013.02.005.

Abdissa, N., Induli, M., Fitzpatrick, P., Alao, J., Sunnerhagen, P., Landberg, G., Yenesew, A., Erdelyi, M., 2014. Cytotoxic quinones from the roots of *Aloe dawei*. Molecules 19 (3), 3264–3273. https://doi.org/10.3390/molecules19033264.

Abdissa, N., Gohlke, S., Frese, M., Sewald, N., 2017. Cytotoxic compounds from *Aloe megalacantha*. Molecules 22 (7), 1136. https://doi.org/10.3390/molecules22071136.

Abera, B., 2014. Medicinal plants used in traditional medicine by Oromo people, Ghimbi District, Southwest Ethiopia. J. Ethnobiol. Ethnomed. 10 (1), 40. https://doi.org/10.1186/1746-4269-10-40.

Adhami, H.R., Viljoen, A.M., 2015. Preparative isolation of biomarkers from the leaf exudate of *Aloe ferox* ("*Aloe* bitters") by high performance counter-current chromatography. Phytochem. Lett. 11, 321–325. https://doi.org/10.1016/j.phytol.2014.07.001.

Al-Oqail, M.M., El-Shaibany, A., Al-Jassas, E., Al-Sheddi, E.S., Al-Massarani, S.M., Farshori, N.N., 2016. *In vitro* anti-proliferative activities of *Aloe perryi* flowers extract on human liver, colon, breast, lung, prostate and epithelial cancer cell lines. Pakistan J. Pharma. Sci. 29 (2 Suppl), 723–729 https://pubmed.ncbi.nlm.nih.gov/27113311/.

Ayana, N.A., 2015. Phytochemical investigation of four asphodelaceae plants for antiplasmodial principles. Erepository.uonbi.ac.ke. http://erepositoryuonbi.ac.ke/handle/11295/95495.

Belayneh, A., Demissew, S., Bussa, N.F., Bisrat, D., 2020. Ethnomedicinal and bio-cultural importance of *Aloes* from south and east of the Great Rift Valley floristic regions of Ethiopia. Heliyon 6, (6). https://doi.org/10.1016/j.heliyon.2020.e04344 e04344.

Berhanu, E., Dagne, E., 1984. Aloe-emodin acetate, an anthraquinone derivative from leaves of *Kniphofia foliosa*. Planta Med. 50 (6), 523–524. https://doi.org/10.1055/s-2007-969790.

Blitzke, T., Porzel, A., Masaoud, M., Schmidt, J., 2000. A chlorinated amide and piperidine alkaloids from *Aloe sabaea*. Phytochemistry 55 (8), 979–982. https://doi.org/10.1016/S0031-9422(00)00269-7.

Bringmann, G., Mutanyatta-Comar, J., Knauer, M., Abegaz, B.M., 2008. Knipholone and related 4-phenylanthraquinones: Structurally, pharmacologically, and biosynthetically remarkable natural products. Nat. Prod. Rep. 25 (4), 696–718. https://doi.org/10.1039/b803784c.

Bula, K.O., Baressa, A.E., 2017. *Aloes* of Ethiopia: a Review on Uses and Importance of *Aloes* in Ethiopia. Int. J. Plant Biol. Res. https://agrisfao.org/agris-search/search.do?recordID = US2018G00051.

Chekole, G., Asfaw, Z., Kelbessa, E., 2015. Ethnobotanical study of medicinal plants in the environs of Tara-gedam and Amba remnant forests of Libo Kemkem District, northwest Ethiopia. J. Ethnobiol. Ethnomed. 11 (1). https://doi.org/10.1186/1746-4269-11-4.

Dagne, E., 1996. Review of the chemistry of *Aloes* of Africa. Bull. Chem. Soc. Ethiop. 10 (1). https://doi.org/10.4314/bcse.v10i1.

Dagne, E., Yenesew, A., 1993. Knipholone anthrone from *Kniphofia foliosa*. Phytochemistry 34 (5), 1440–1441. https://doi.org/10.1016/0031-9422(91)80048-6.

Dagne, E., Yenesew, A., Asmellash, S., Demissew, S., Mavi, S., 1994. Anthraquinones, pre-anthraquinones and isoeleutherol in the roots of *Aloe* species. Phytochemistry 35 (2), 401–406. https://doi.org/10.1016/S0031-9422(00)94771-X.

Dagne, E., Bisrat, D., Viljoen, A., Van Wyk, B.E., 2000. Chemistry of *Aloe* species. Curr. Org. Chem. 4 (10), 1055–1078.

Dagne, E., Steglich, W., 1984. Knipholone: a unique anthraquinone derivative from *Kniphofia foliosa*. Phytochemistry 23 (8), 1729–1731. https://doi.org/10.1016/S0031-9422(00)83479-2.

Dai, Y., Harinantenaina, L., Bowman, J.D., Da Fonseca, I.O., Brodie, P.J., Goetz, M., Cassera, M.B., Kingston, D.G.I., 2014. Isolation of antiplasmodial anthraquinones from *Kniphofia ensifolia*, and synthesis and structure-activity relationships of related compounds. Bioorg. Med. Chem. 22 (1), 269–276. https://doi.org/10.1016/j.bmc.2013.11.032.

Demissew, S., Nordal, I., 2010. *Aloes* and Lilies of Ethiopia and Eritrea. Shama Books, 42–110.

Dessalegn, F., 2013. Study on the populations of an endemic *Aloe* species (*A. gilbertii* Reynolds) in Ethiopia. Eng. Sci. Technol.: Int. J. 3 (3), 562–576.

Edwards, S., Demissew, S., Hedberg, I., 1997. Flora of Ethiopia and Eritrea. The National Herbareum, Addis Ababa Universtiy, Hydrocharitaceae to Arecaceae.

Egesie, U.G., Chima, K.E., Galam, N.Z., 2011. Anti-inflammatory and analgesic effects of aqueous extract of *Aloe vera (Aloe barbadensis)* in rats. African J. Biomed. Res. 14 (3), 209–212.

Feilcke, R., Arnouk, G., Raphane, B., Richard, K., Tietjen, I., Andrae-Marobela, K., Erdmann, F., Schipper, S., Becker, K., Arnold, N., Frolov, A., Reiling, N., Imming, P., Fobofou, S.A.T., 2019. Biological activity and stability analyses of knipholone anthrone, a phenyl anthraquinone derivative isolated from *Kniphofia foliosa* Hochst. J. Pharm. Biomed. Anal. 174, 277–285. https://doi.org/10.1016/j.jpba.2019.05.065.

Gebru, M., 2010. Phytochemical and antiplasmodial investigation of rhamnus prinoides and kniphofia foliosa. Erepository.uonbi.ac.ke. http://erepositoryuonbi.ac.ke/handle/11295/11592.

Geremedhin, G., Bisrat, D., Asres, K., 2014. Isolation, characterization and *in vivo* antimalarial evaluation of anthrones from the leaf latex of *Aloe percrassa* Todaro. J. Nat. Remedies 14 (2), 119–125 http://52.172.159.94/index.php/jnr/article/view/54172.

Habtemariam, S., 2007. Antioxidant activity of Knipholone anthrone. Food Chem. 102 (4), 1042–1047. https://doi.org/10.1016/j.foodchem.2006.06.040.

Habtemariam, S., 2010. Knipholone anthrone from *Kniphofia foliosa* induces a rapid onset of necrotic cell death in cancer cells. Fitoterapia 81 (8), 1013–1019. https://doi.org/10.1016/j.fitote.2010.06.021.

Hiruy, M., Bisrat, D., Mazumder, A., Asres, K., 2019. Two chromones with antimicrobial activity from the leaf latex of *Aloe monticola* Reynolds. Nat. Prod. Res. 35 (6), 1052–1056. https://doi.org/10.1080/14786419.2019.1614581.

Hotti, H., Rischer, H., 2017. The killer of Socrates: Coniine and related alkaloids in the plant kingdom. Molecules 22 (11), 1962. https://doi.org/10.3390/molecules22111962.

Induli, M., Gebru, M., Abdissa, N., Akala, H., Wekesa, I., Byamukama, R., Heydenreich, M., Murunga, S., Dagne, E., Yenesew, A., 2013. Antiplasmodial quinones from the rhizomes of *Kniphofia foliosa*. Nat. Prod. Commun. 8 (9), 1261–1264. https://doi.org/10.1177/1934578x1300800920.

Jesikha, M., 2012. Evaluation of larvicidal efficacy of *Aloe vera* extract against *Musca domestica*. IOSR J. Environ. Sci., Toxicol. Food Technol. 2 (2), 01–03. https://doi.org/10.9790/2402-0220103.

Kametani, S., Kojima-Yuasa, A., Kikuzaki, H., Kennedy, D.O., Honzawa, M., Matsui-Yuasa, I., 2007. Chemical constituents of cape *Aloe* and their synergistic growth-inhibiting effect on ehrlich ascites tumor cells. Biosci. Biotechnol. Biochem. 71 (5), 1220–1229. https://doi.org/10.1271/bbb.60659.

Karagianis, G., Viljoen, A., Waterman, P.G., 2003. Identification of major metabolites in *Aloe littoralis* by high-performance liquid chromatography-nuclear magnetic resonance spectroscopy. Phytochem. Anal. 14 (5), 275–280. https://doi.org/10.1002/pca.714.

Koroch, A.R., Juliani, H.R., Simon, J.E., 2009. Biology and chemistry of the genus *Aloe* from Africa. ACS Symp. Ser. 1021, 171–183. https://doi.org/10.1021/bk-2009-1021.ch009.

Kumar, S., 2017. Evaluating antimicrobial activity of *Aloe vera* plant extract in human life. Biomed. J. Scient. Tech. Res. 1 (7), 1854–1856.

Malmir, M., Serrano, R., Silva, O., 2017. Anthraquinones as potential antimicrobial agents-A review. Novel bioknowledge and educational programs. Formatex, Antimicrobial research, pp. 55–61.

Matasyoh, J.C., Wathuta, E.M., Kariuki, S.T., Chepkorir, R., Kavulani, J., 2008. *Aloe* plant extracts as alternative larvicides for mosquito control. Afr. J. Biotechnol. 7 (7), 912–915. https://doi.org/10.4314/ajb.v7i7.58574.

Meshesha, M., Deyou, T., Tedla, A., Abdissa, N., 2017. Chemical constituents of the roots of *Kniphofia isoetifolia* Hochst. and evaluation for antibacterial activity. J. Pharm. Pharmacogn. Res. 5 (6), 345–353.

Mothana, R., Gruenert, R., Bednarski, P.J., Lindequist, U., 2009. Evaluation of the *in vitro* anticancer, antimicrobial and antioxidant activities of some Yemeni plants used in folk medicine. Pharmazie 64 (4), 260–268. https://doi.org/10.1691/ph.2009.8789.

Mpiana, P. T., Ngbolua, K.-T.-N., Tshibangu, D. S. T., Kilembe, J. T., Gbolo, B. Z., Mwanangombo, D. T., Inkoto, C. L., Lengbiye, E. M., Mbadiko, C. M., Matondo, A., Bongo, G. N., & Tshilanda, D. D. (2020). *Aloe vera* (L.) Burm. F. as a potential anti-covid-19 plant: A mini-review of its antiviral activity. *European Journal of Medicinal Plants*, 86–93. https://doi.org/10.9734/ejmp/2020/v31i830261.

Mugomeri, E., Chatanga, P., Raditladi, T., Makara, M., Tarirai, C., 2016. Ethnobotanical study and conservation status of local medicinal plants: towards a repository and monograph of herbal medicines in Lesotho. Afr. J. Tradit. Complement. Altern. Med. 13 (1), 143–156.

Mwale, M., Masika, P.J., 2010. Analgesic and anti-inflammatory activities of *Aloe ferox* Mill. aqueous extract. African J. Pharm. Pharmacol. 4 (6), 291–297.

Achieng, O.I. (2009). Antiplasmodial anthraquinones and benzaldehyde derivatives from the roots of *kniphofia thomsonii*. https://profiles.uonbi.ac.ke/achiengimma/files/ima-abstract.pdf.

Okamura, N., Hine, N., Tateyama, Y., Nakazawa, M., Fujioka, T., Mihashi, K., Yagi, A., 1998. Five chromones from *Aloe vera* leaves. Phytochemistry 49 (1), 219–223. https://doi.org/10.1016/S0031-9422(97)01071-6.

Omer, H., Abakar, M., Ea Bakhiet, S., Hagir, C., Musa Abakar, O., Musa Abakar, H., Satti, R., Abadi, M., 2017. Antimicrobial activity and minimum inhibitory concentration of *Aloe vera* sap and leaves using different extracts. J. Pharmacogn. Phytochem. 6 (3), 298–303 https://www.phytojournal.com/archives/2017/vol6issue3/PartF/6-3-14-403.

Puia, A., Puia, C., Moiș, E., Graur, F., Fetti, A., Florea, M., 2021. The phytochemical constituents and therapeutic uses of genus *Aloe*: a review. Notulae Botanicae Horti Agrobotanici Cluj-Napoca 49 (2), 1–16.

Quispe, C., Villalobos, M., Bórquez, J., Simirgiotis, M., 2018. Chemical composition and antioxidant activity of *Aloe vera* from the Pica Oasis (Tarapaca Chile) by UHPLC-Q/Orbitrap/MS/MS. J. Chem. 2018. https://doi.org/10.1155/2018/6123850.

Ramarumo, L.J., Maroyi, A., Tshisikhawe, M.P., 2019. *Warburgia salutaris* (G. Bertol.) Chiov.: An endangered therapeutic plant used by the Vhavenda ethnic group in the Soutpansberg, Vhembe Biosphere Reserve, Limpopo province, South Africa. *Res. J. Pharm. Technol.* 12 (12), 5893. https://doi.org/10.5958/0974-360x.2019.01022.9.

Ripperger, H., Schreiber, K., Budzikiewicz, H., 1970. Putrescine amides from *Kniphofia* species. J. Pract. Chem. 312 (3), 449–455. https://doi.org/10.1002/prac.19703120308.

Sagbo, I., Mbeng, W., 2018. Plants used for cosmetics in the Eastern Cape Province of South Africa: a case study of skin care. Pharmacogn. Rev. 12 (24), 139–156.

Salehi, B., Albayrak, S., Antolak, H., Kręgiel, D., Pawlikowska, E., Sharifi-Rad, M., Uprety, Y., Fokou, P.V.T., Yousef, Z., Zakaria, Z.A., Varoni, E.M., Sharopov, F., Martins, N., Iriti, M., Sharifi-Rad, J., 2018. *Aloe* genus plants: From farm to food applications and phytopharmacotherapy. Int. J. Mol. Sci. 19 (9). https://doi.org/10.3390/ijms19092843.

Saniasiaya, J., Salim, R., Mohamad, I., Harun, A., 2017. Antifungal effect of Malaysian *Aloe vera* leaf extract on selected fungal species of pathogenic otomycosis species in *in vitro* culture medium. Oman Med. J. 32 (1), 41–46. https://doi.org/10.5001/omj.2017.08.

Schmelzer, G. H., Gurib-Fakim, A., Arroo, R., Bosch, C. H., Ruijter, A. de, Simmonds, M. S. J., Lemmens, R. H. M. J., & Oyen, L. P. A. (2008). Plant Resources of Tropical Africa 11(1) : Medicinal plants 1. In *research.wur.nl*. PROTA Foundation [etc.]. https://research.wur.nl/en/publications/plant-resources-of-tropical-africa-111-medicinal plants-1.

Sema, D. K., Meli Lannang, A., Tatsimo, S. J. N., Mujeeb-ur-Rehman, Yousuf, S., Zoufou, D., Iqbal, U., Wansi, J. D., Sewald, N., & Choudhary, M. I. (2018). New indane and naphthalene derivatives from the rhizomes of *Kniphofia reflexa* Hutchinson ex Codd. *Phytochemistry Letters*, *26*(May), 78–82. https://doi.org/10.1016/j.phytol.2018.05.025

Smith, G. F., & Wyk, B. E. (1998). Asphodelaceae. In *flowering plants· Monocotyledons* (pp. 130-140). Springer, Berlin, Heidelberg.

Sonam, S.K., Archana, T., 2015. Antibacterial efficacy of *Aloe* species on pathogenic bacteria. Int. J. Sci. Technol. Manage. 4 (1), 143–151.

Surjushe, A., Vasani, R., Saple, D., 2008. *Aloe vera*: A short review. Indian Journal of Dermatology 53 (4), 163. https://doi.org/10.4103/0019-5154.44785.

Tadesse, M., Mesfin, B., 2010. A review of selected plants used in the maintenance of health and wellness in Ethiopia. Ethiopian E-J. Res. Inov. Foresight 2 (1), 85–102.

Van Heerden, F.R., Viljoen, A.M., van Wyk, B.-E., 2000. 6′-O-Coumaroylaloesin from *Aloe castanea*-a taxonomic marker for *Aloe* section Anguialoe. Phytochemistry 55 (2), 117–120. https://doi.org/10.1016/s0031-9422(00)00252-1.

Waithaka, P.N., Gathuru, E.M., Githaiga, B.M., Kazungu, R.Z., 2018. Antimicrobial properties of *Aloe vera*, *Aloe volkensii* and *Aloe secundiflora* from Egerton University. Acta Scient. Microbiol. 1 (5), 06–10.

Wube, A.A., Bucar, F., Asres, K., Gibbons, S., Rattray, L., Croft, S. L., 2005. Antimalarial compounds from *Kniphofia foliosa* roots. Phytother. Res. 19 (6), 472–476. https://doi.org/10.1002/ptr.1635.

Wube, A.A., Bucar, F., Asres, K., Gibbons, S., Adams, M., Streit, B., Bodensieck, A., Bauer, R., 2006. Knipholone, a selective inhibitor of leukotriene metabolism. Phytomedicine 13 (6), 452–456. https://doi.org/10.1016/j.phymed.2005.01.012.

Yadeta, N.C., 2019. Phytochemical investigation and antioxidant activity of root extract of *Aloe gilbertii* Reynolds, from Konso, Southern Ethiopia. Am. J. Appl. Chem. https://doi.org/10.11648/J.AJAC.20190705.11.

Yenesew, A., Dagne, E., Müller, M., Steglich, W., 1994. An anthrone, an anthraquinone and two oxanthrones from *Kniphofia foliosa*. Phytochemistry 37 (2), 525–528. https://doi.org/10.1016/0031-9422(94)85092-5.

Yineger, H., Kelbessa, E., Bekele, T., Lulekal, E., 2007. Ethnoveterinary medicinal plants at Bale Mountains National Park, Ethiopia. *J. Ethnopharmacol.* 112 (1), 55–70. https://doi.org/10.1016/j.jep.2007.02.001.

Yineger, H., Kelbessa, E., Bekele, T., Lulekal, E., 2008. Plants used in traditional management of human ailments at Bale Mountains National Park, South Eastern Ethiopia. J. Med. Plants Res. 2 (6), 132–153.

Zenebe, G., Zerihun, M., Solomon, Z., 2012. An ethnobotanical study of medicinal plants in Asgede Tsimbila District, Northwestern Tigray, Northern Ethiopia. *Ethnobotany Res. Appl.* 10, 305–320. https://doi.org/10.17348/era.10.0.305-320.