

See discussions, stats, and author profiles for this publication at: <https://www.researchgate.net/publication/276358260>

# Chromolaena odorata (L.) R.M. King & H. Rob. (Asteraceae) in sub-Saharan Africa: A synthesis and review of its medicinal potential

Article in *Journal of ethnopharmacology* · May 2015

DOI: 10.1016/j.jep.2015.04.057 · Source: PubMed

CITATIONS

29

READS

986

4 authors, including:



**Aitebiremen Gift Omokhua**  
University of KwaZulu-Natal

13 PUBLICATIONS 61 CITATIONS

[SEE PROFILE](#)



**Lyndy McGaw**  
University of Pretoria

257 PUBLICATIONS 3,821 CITATIONS

[SEE PROFILE](#)



**Johannes van Staden**  
University of KwaZulu-Natal, South Africa, Pietermaritzburg

409 PUBLICATIONS 9,363 CITATIONS

[SEE PROFILE](#)

Some of the authors of this publication are also working on these related projects:



Determining the antimycobacterial properties of *Psychotria* species [View project](#)



Evaluation of biological activity of some South African alien invasive plants against pathogens causing infection in the CNS of immunocompromised patients [View project](#)



# *Chromolaena odorata* (L.) R.M. King & H. Rob. (Asteraceae) in sub-Saharan Africa: A synthesis and review of its medicinal potential

Aitebiremen G. Omokhua, Lyndy J. McGaw, Jeffrey F. Finnie, Johannes Van Staden\*



Research Centre for Plant Growth and Development, School of Life Sciences, University of KwaZulu-Natal Pietermaritzburg, Private Bag X01, Scottsville 3209, South Africa

## ARTICLE INFO

### Article history:

Received 12 February 2015

Received in revised form

28 April 2015

Accepted 30 April 2015

### Keywords:

*Chromolaena odorata*

Sub-Saharan Africa

Biotype

Pharmacology

Weed

## ABSTRACT

**Ethnopharmacological relevance:** *Chromolaena odorata* (L.) R.M. King & H. Rob. (Asteraceae) is a scrambling perennial shrub that originated in the Americas, but is now common in sub-Saharan Africa, Asia and Oceania, where it has become a serious weed. The species, particularly the biotype found in Asia and West Africa, has many ethnopharmacological uses, including treatment of malaria, wounds, diarrhoea, skin infection, toothache, dysentery, stomach ache, sore throat, convulsions, piles, coughs and colds. Furthermore, no attempt has been made to synthesise and review the available literature on the usefulness of the plant in the sub-Saharan African region, hence this paper examines the beneficial attributes of *C. odorata* in sub-Saharan Africa.

**Material and methods:** Published information on the species was gathered by the use of different database platforms, including Google Scholar, ScienceDirect, SciFinder and Scopus.

**Results:** Records indicate that two biotypes of *C. odorata* are present in sub-Saharan Africa viz. the more widespread Asian/West African *C. odorata* biotype (AWAB) and the southern African biotype (SAB). While the usefulness of the former is well elucidated in the literature, such information on the latter is still scarce. Although the importance of AWAB *C. odorata* as a fallow species and as a soil fertility improvement plant in the slash and burn rotation system of agriculture in West Africa is increasingly being recognised, its usage in traditional medicinal practice is far more appreciated. The species has a wide range of ethnopharmacological uses, possibly because of the presence of flavonoids, essential oils, phenolics, tannins and saponins. The plant is reported to have antibacterial, anti-inflammatory, antioxidant, anthelmintic, antifungal, cytotoxic, anticonvulsant, antiprotozoal, antispasmodic, antipyretic and analgesic properties.

**Conclusion:** While the results of this review suggest that the AWAB plant can be exploited as an alternative to other threatened plant species known to possess similar medicinal potential, the medicinal and pharmacological potential of the SAB plant remains to be established. Further studies on the phytochemistry and pharmacological properties of the SAB plants will not only advance our knowledge of ethnobotany and ethnomedicine, but may also improve the health and knowledge of the local people.

© 2016 Published by Elsevier Ireland Ltd.

## 1. Introduction

*Chromolaena odorata* (= *Eupatorium odoratum*) (Asteraceae) is an invasive perennial shrub native to the Americas (McFadyen, 1989). It is considered to be a significant economic and ecological burden to many tropical and sub-tropical regions of the world where it impacts negatively on agriculture, biodiversity and livelihoods (Zachariades et al., 2009; Uyi and Igbinsosa, 2013). Following its introduction into West Africa in the 1930s (Ivens, 1974) and South Africa in the 1940s (Zachariades et al., 2011), the species

\* Correspondence to: Research Centre for Plant Growth and Development, School of Life Sciences, University of KwaZulu-Natal, Private Bag X01, Scottsville 3209, South Africa. Tel.: +27 33 260 5130.

E-mail address: [rcpgd.ukzn@ac.za](mailto:rcpgd.ukzn@ac.za) (J. Van Staden).

<http://dx.doi.org/10.1016/j.jep.2015.04.057>

0378-8741/© 2016 Published by Elsevier Ireland Ltd.

has spread into many sub-Saharan African countries (Timbilla et al., 2003; Uyi and Igbinsosa, 2013; Zachariades et al., 2013). The biology of *C. odorata*, and aspects of its ecology, has been studied (Gautier, 1992; Witkowski and Wilson, 2001; Rambuda and Johnson, 2004) and reviewed in Timbilla et al. (2003) and Zachariades et al. (2009). The plant grows best in sunny or open areas such as roadsides, abandoned fields, pastures, and disturbed forests, but tolerates semi-shade conditions. A single shrub can produce as many as 80 000 seeds in one season (Witkowski and Wilson, 2001). The species has the tenacity to invade human-induced disturbed and undisturbed lands, posing a significant economic and ecological burden in many countries in its introduced ranges.

The status of *C. odorata* as an agricultural and environmental weed has been a subject of burgeoning concern in the past four

decades in west and southern sub-Saharan Africa, probably because of its invasiveness in agro-ecosystems and conservation areas (Ivens, 1974, Lucas 1989; Goodall and Erasmus, 1996; Timbilla et al., 2003; Uyi et al., 2014). The invasive success of *C. odorata* is thought to depend upon a combination of several factors such as; (i) high reproductive capacity; (ii) high growth and net assimilation rates; (iii) its capacity to suppress native vegetation through competition for light and allelopathic properties; and (iv) its ability to grow in many soil types and in many climatic zones (Zachariades et al., 2009; Uyi et al., 2014).

While *C. odorata* has been declared a 'Category 1' weed under the Conservation of Agricultural Resources Act (CARA) and the National Environmental Management Biodiversity Act (NEMBA) on Alien and Invasive Species List in South Africa because of its invasiveness in the north-eastern parts of the country (Goodall and Erasmus, 1996; Nel et al., 2004; Zachariades et al., 2011), the situation in West Africa remains contentious despite numerous research reports and the perceived usefulness of the plant in the latter region (Uyi et al., 2014). In view of its coverage of large areas, and its invasive propensity, the use of chemical, mechanical and other conventional methods of controlling the weed have proven not to be sustainable (Timbilla et al., 2003; Zachariades et al., 2009; Uyi and Igbinosa, 2013). Hence, the use of biological control methods (using natural enemies to feed on the species) has been advocated as an important long-term management strategy for controlling the weed (Seibert, 1989).

Despite its invasive or weedy status, *C. odorata* is seen by locals in parts of Asia and sub-Saharan Africa as a plant with potential medicinal properties. The species has also been the subject of numerous ethnobotanical and ethnopharmacological investigations in some countries in West Africa and southeast Asia (Phan et al., 1998; Akinmoladun et al., 2007; Idu and Onyibe, 2007; Raina et al., 2008; Panda et al., 2010; Anyasor et al., 2011; Vijayaraghavan

et al., 2013). While the negative impact of *C. odorata* has received considerable attention in sub-Saharan Africa (Ivens, 1974; Lucas, 1989; Goodall and Erasmus, 1996; Zachariades et al., 2011; Uyi and Igbinosa, 2013), no attempt has been made to synthesise or review literature on the medicinal potential of *C. odorata* in the sub-Saharan African countries. With the exception of the limited reviews on *C. odorata* by Chakraborty et al. (2011) and Vaisakh and Pandey (2012) in Asia, we are not aware of any study that has extensively reviewed the medicinal potential of this plant species worldwide. Furthermore, studies on the medicinal attributes of *C. odorata* in Africa are beginning to be explored and some important medicinal properties of the plant have been documented, supporting the necessity for a comprehensive evaluation of the species. This paper reviews the beneficial attributes of *C. odorata* in some sub-Saharan African countries and discusses the medicinal importance, phytochemistry and bioactivities of the plant.

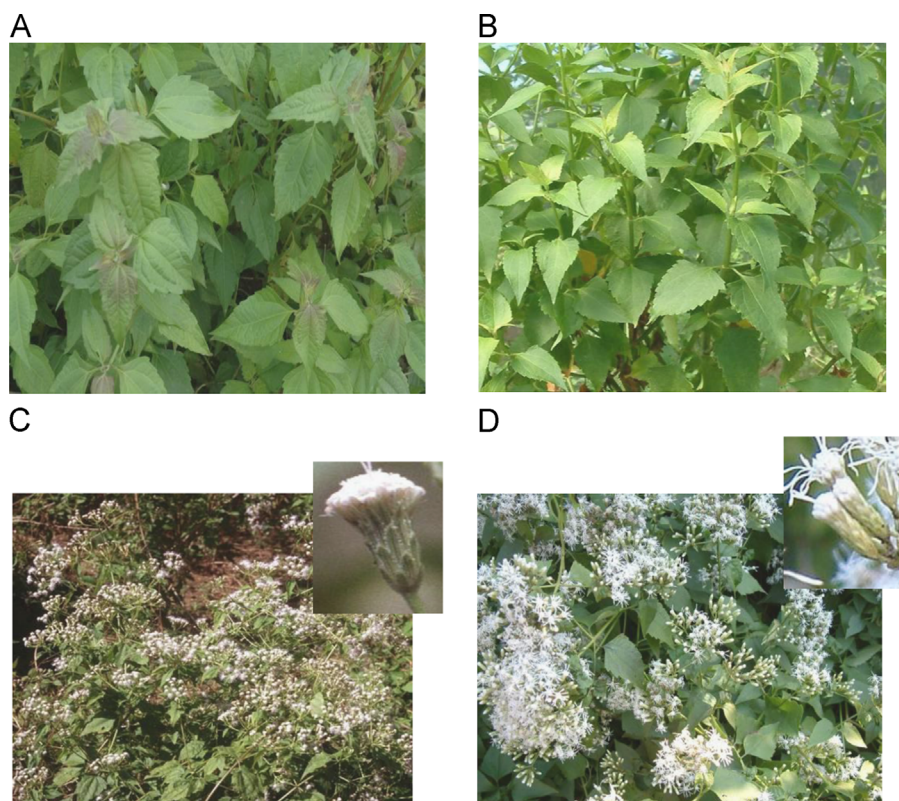
## 2. Methods

Published information on *C. odorata* was gathered using different database platforms, including Google Scholar, ScienceDirect, SciFinder and Scopus. All papers that mention *C. odorata* and its weed status, distribution or beneficial attributes in any capacity (for example spread, medicinal potential and invasive status) were included in the selection process.

## 3. Results and discussion

### 3.1. Genetic and morphological dissimilarity in *C. odorata*

Two biotypes of *C. odorata* are known in their invasive range of distribution, viz. the Asian/West African biotype (AWAB) and the



**Fig. 1.** (A and C) Leaves and Flowers of the Asian/West African Biotype. (B and D) Leaves and Flowers of the Southern African Biotype. (Fig. 1 A and C photos were taken by Colin Wilson, Parks and Wildlife Commission of the Northern Territory, Australia; Fig. 1B and D photos were taken by Costas Zachariades, ARC-Plant Protection Research Institute, South Africa).

southern African biotype (SAB). The AWAB which is the most widely spread form found in West and Central sub-Saharan Africa, Asia, India, and Oceania, originated from Trinidad and Tobago and adjacent areas (Yu et al., 2014), while the SAB found only in southern sub-Saharan Africa countries is thought to have originated from Jamaica or Cuba (Paterson and Zachariades, 2013). The two biotypes are known to differ in morphology, genetics and aspects of their ecology (Paterson and Zachariades, 2013).

The differences between AWAB and SAB plants have been elucidated (C. Zachariades, ARC-PPRI, South Africa, unpublished data). The sub-Saharan southern African biotype of *C. odorata* is substantially different from the widespread invasive biotype found in Asia, West and Central sub-Saharan Africa in the following ways:

- (i) the leaves of the AWAB are usually large with fine hairs giving a soft texture particularly to younger leaves, with a grey-green to dark-green colour, but often purple at the young stage especially when growing in the sun, while the leaves of the SAB are distinctly small and smooth, with a dark-green colour when growing in semi-shade, but yellow-green in the sun and red when young (Fig. 1a and b),
- (ii) the stems of the AWAB are hairy, with a grey-green to dark green colour, while those of the SAB are largely smooth and yellow-green in colour,
- (iii) the AWAB have broad individual flowers with a pale lilac colour, bracts have sharp tips and are lax around the flower-head, while the SAB flowers are often narrow with whitish colour, bracts having round tips and are tight around the flower-head (Fig. 1c and d),
- (iv) the branches of the AWAB are not rigid, while the SAB has upright posture especially young growth in dense stands, and
- (v) the AWAB are more adapted to tropical conditions, and may be more fire resistant, having a tendency to re-grow from the crown, while the SAB may be more cold tolerant and more susceptible to fire.

### 3.2. Beneficial attributes and medicinal potential of *C. odorata*

Both biotypes of *C. odorata* have been implicated in negative impacts on agriculture, human livelihoods, biodiversity and ecotourism in its introduced range where it has become invasive. Nevertheless, the usefulness of *C. odorata* as a fallow plant and its soil improvement properties have been recognised (Tian et al.,

1998; Akobundu et al., 1999; Tian et al., 2005; Koutika and Rainey, 2010). Biogas can be produced from the plant by anaerobic digestion (Jagadeesh et al., 1990). The species is reported to be a good bioremediating and phytoremediating agent in heavy metal and crude oil polluted soils (Anoliefo et al., 2003; Agunbiade and Fawale, 2009; Alcantara et al., 2013).

*C. odorata* leaves are a good source of protein, ash, carbohydrate, fibre and energy (Nwinuka et al., 2009). Apori et al. (2000) suggested the use of *C. odorata* as a protein supplement in ruminant feeds because of the high crude protein content in the plant, although further investigation may be required to rule out toxicity effects in livestock. The plant is eaten by locals in southern parts of Nigeria as a vegetable (A.G. Omokhua, personal observation), probably because of its high nutritional content.

*C. odorata* is also seen as a plant with immense medicinal potential in Southeast Asia and in some countries in West Africa (Chakraborty et al., 2011; Vaisakh and Pandey, 2012). Medicinal plants are defined as those plants of which one or more of the organs contain substances that can be used for therapeutic purposes, or which can be used as precursors for the synthesis of useful drugs (Sofowora, 1982). Though *C. odorata* has been known for its negative impact, its potential medicinal uses have been documented (Owoyele et al., 2005). Traditional healers in some parts of sub-Saharan African countries exploit the plant as a source of medicine for curing different ailments.

#### 3.2.1. Traditional usage

*C. odorata* is used as a source of medicine in traditional medicinal practice in West Africa and countries in Asia. The plant is known for its medicinal properties especially in the treatment of wounds (Phan et al., 2001). The traditional medicinal usage of *C. odorata* in some sub-Saharan countries is detailed in Table 1. Although several traditional uses of this plant have been recognised by locals in a number of West African countries and even in Cameroon, there is currently no known traditional usage for this plant in eastern and southern Africa. A number of scenarios or hypotheses may partly explain the non-usage of the plant by traditional medicinal practitioners in these regions. Firstly, the recent arrival of the species into eastern Africa might suggest that traditional medicinal practitioners or locals are yet to fully understand the benefits of the plant, as recently introduced plant species may not be utilised by locals. Secondly, knowledge of the medicinal usefulness of the plant may elude practitioners or locals in South Africa because the plant is restricted to very limited parts

**Table 1**  
Ethnopharmacological usage of the Asian/West African *Chromolaena odorata* biotype in its distribution range.

Category of use	Description of traditional usage	References
<b>Coughs and cold remedy</b>	The plant is squeezed in water and the extract is taken to cure colds and coughs	Morton (1981) and Timbilla et al. (2003)
<b>Skin diseases</b>	The leaf is squeezed in water to bath	Morton (1981)
<b>Wounds and antiseptic</b>	The leaves are squeezed and applied to the wound	Adjanohoun and Ake-Assi (1979) and Inya-Agha et al. (1987)
<b>Dysentery</b>	The leaves are squeezed and taken as a tonic	Gill (1992)
<b>Headache</b>	The leaves are squeezed and taken as a tonic	Gill (1992)
<b>Toothache</b>	The leaves are squeezed and the juice is applied to the aching part	Gill (1992)
<b>Malaria fever</b>	Adecoction of the leaves with <i>Azadiracta indica</i> is prepared and the water is taken	Ayensu (1978), Gill (1992), and Idu and Onyibe (2007)
<b>Antiseptic</b>	The juice of the leaves, sometimes mixed with water, is used to stop bleeding	Gill (1992)
<b>Stomach problems</b>	Fresh leaves are squeezed with water and the juice is taken as tonic	Hoeyers and M'boob (1996) and Idu and Onyibe (2007)
<b>Antiseptic and haemostatics</b>	Fresh juice from the leaves is used to arrest bleeding in fresh cuts and nose bleeding	Phan et al. (2001) and Idu and Onyibe (2007)
<b>Diarrhoea</b>	The leaves are squeezed with water and the decoction is taken as a tonic	Amatya and Tuladhar (2011) and Bhargava et al. (2011)
<b>Skin eruption</b>	The fresh leaves are squeezed and the juice is applied to affected areas of skin	Amatya and Tuladhar (2011) and Bhargava et al. (2011)
<b>Fungal infections</b>	The leaves are squeezed and taken as juice	Ngono et al. (2006)
<b>Stomach ulcers</b>	The leaves are squeezed and the juice is combined with honey and taken as a tonic	Nur Jannah et al. (2006)
<b>Skin infection</b>	The juice is squeezed out from the leaves and applied to affected areas	Owoyele et al. (2005)

of the country. Thirdly, ethnobotanical studies on indigenous knowledge of the medicinal usage of the plant are still scanty. Finally, the *C. odorata* biotype invasive in South Africa may not have (or may have fewer) medicinal properties compared with the AWAB which has been recorded to have medicinal usage by locals in West Africa and Southeast Asia. Due to the documented medicinal potential of this plant in a number of West African countries, studies on the invasive biotype of the species in South Africa are needed to either validate or invalidate the above conjectures.

### 3.2.2. Secondary metabolites reported in *C. odorata*

**3.2.2.1. Phenolics and flavonoids.** Phenolic compounds such as protocatechuic, p-coumaric, ferulic, p-hydroxybenzoic and vanillic acids have been isolated from the Asian/West African *C. odorata* biotype and these phenolic compounds from AWAB help protect cultured skin cells and retard oxidative degradation of lipids (Phan et al., 2001). Whether these phenolic compounds are also present in the southern African *C. odorata* biotype remains to be established.

The known flavonoids isolated from *C. odorata* are detailed in Table 2. Some of the flavonoids listed in Table 2 are only found in *C. odorata* and a few other plant species. For example, quercetagenin-6,4'-dimethyl ether, a very rare flavonoid, has been detected in *C. odorata* by Wollenweber et al. (1995). This flavone has only been found in *Brickella laciniata* (Timmermann et al., 1979) and in two *Arnica* species (Merfort, 1985). Aromadendrin-7,4'-dimethyl

ether, which has also been detected in *C. odorata* (Wollenweber et al., 1995), has only been isolated from the bark of *Cephalanthus spathelliferus* (Lima and Polonsky, 1973). Taxifolin-7-methyl ether has been reported in *Prunus puddum*, *Artemisia glutinosa* and *Inula viscosa* (Wollenweber et al., 1991). This further underscores the medicinal potential of *C. odorata* (Table 3).

There is a possibility that *C. odorata* can be effective against human small cell lung and breast cancer as studies carried out have demonstrated the presence of important compounds such as luteolin and acacetin which can act against cancer (Suksamrarn et al., 2004). The compound 2-hydroxy-4',5',6,4-tetramethoxy chalcone extracted from *C. odorata* leaves has been found to possess both cytotoxic and anticlonogenic actions against a variety of cancer cell lines (Kouamé et al., 2013). Flavonoid compounds such as eriodictyol-7-4'-dimethyl ether, naringenin-4'-methyl ether and 2',4-dihydroxy-4',5',6',-trimethoxy chalcone have high efflux inhibitory action against methicillin-resistant *Staphylococcus aureus* (MRSA), suggesting they can be good efflux inhibitors for MRSA (Johari et al., 2012).

**3.2.2.2. Essential oils.** The dry stems and leaves of *C. odorata* are known to be very rich in essential oils (Moni and Subramoniam, 1960). Research carried out on the bioactivity of essential oils isolated from the leaves of *C. odorata* by Inya-Agha et al. (1987) and Owolabi et al. (2010) in Nigeria reported the presence of  $\alpha$ -pinene,  $\beta$ -pinene, germacrene D,  $\beta$ -copaen-4- $\alpha$ -ol,  $\beta$ -carophyllene, geigerene, pregeigerene, cadinene, camphor, limonene

**Table 2**  
Flavonoid compounds isolated from Asian/West African *Chromolaena odorata*.

Semi-systematic name	Trivial name	References
Quercetin-7-methyl ether	Rhamnetin	Wollenweber et al. (1995), Ling et al. (2007), and Johari et al. (2012)
Quercetin-4-methyl ether	Tamarixetin	Wollenweber et al. (1995), Ling et al. (2007), and Johari et al. (2012)
Quercetin-7-4'-dimethyl ether	Ombuin	Wollenweber et al. (1995), Ling et al. (2007), and Johari et al. (2012)
Kaempferol-4'-methyl ether	Kaempferid	Iwu and Chiori (1984), Wollenweber et al. (1995), Ling et al. (2007), and Johari et al. (2012)
Naringenin-4'-methyl ether	Isosakuranetin	Iwu and Chiori (1984), Wollenweber et al. (1995), Ling et al. (2007), and Johari et al. (2012)
Scutellarein-6,4'-dimethyl ether	-	Wollenweber et al. (1995)
Luteolin-3',4'-dimethyl ether	-	Wollenweber et al. (1995)
Quercetin-3'',4'-dimethyl ether	-	Wollenweber et al. (1995)
Naringenin-7,4'-dimethyl ether	-	Wollenweber et al. (1995)
Eriodictyol-7,4'-dimethyl ether	-	Wollenweber et al. (1995), Ling et al. (2007) and Johari et al. (2012)
Aromadendrin-7,4'-dimethyl ether	-	Wollenweber et al. (1995)
2,4-dihydroxy-4',5',6'-trihydroxy chalcone	-	Wollenweber et al. (1995)
2-hydroxy-4',5',6,4-tetramethoxy chalcone	Odoratin	Wollenweber et al. (1995)
Quercetin	-	Wollenweber et al. (1995)
Quercetin-7,3',4'-trimethyl ether	-	Wollenweber et al. (1995)
Kaempferol	-	Wollenweber et al. (1995)
Kaempferol-7-methyl ether	Rhamnocitrin	Wollenweber et al. (1995)
Kaempferol-7,4-dimethyl ether	-	Wollenweber et al. (1995)
Quercetagenin-6,4'-dimethyl ether	Laciniatin	Wollenweber et al. (1995)
Apigenin-4-methyl ether	Acacetin	Wollenweber et al. (1995)
Scutellarein-5,6,7,4'-tetramethyl ether	-	Wollenweber et al. (1995)
5,6,7,3',4'-pentamethoxy flavone	Sinensetin	Wollenweber et al. (1995)
Naringenin-7-methyl ether	Sakuranetin	Iwu and Chiori (1984) and Wollenweber et al. (1995)
Taxifolin-7-methyl ether	Padmatin	Wollenweber et al. (1995), Ling et al. (2007), and Johari et al. (2012)
2-hydroxy-3,4,4',5',6'-pentamethoxy chalcone	-	Wollenweber et al. (1995)
2',4-dihydroxy-4',5',6'-trimethoxy chalcone	-	Barua et al. (1978) and Johari et al. (2012)
4'-OH-5,6,7-trimethoxy flavone	-	Barua et al. (1978)
Scutellarein-tetramethyl ether	-	Barua et al. (1978)
2-OH-4',5',6',4,5-pentamethoxy chalcone	-	Barua et al. (1978)
Quercetagenin-3,5,7,3'-tetramethyl ether	-	Iwu and Chiori (1984)
3-OH-5,6,7,3',4'-pentamethoxy flavone	Marionol	Wollenweber and Roitman (1996)
5-hydroxy-4',7-dimethoxy flavone	-	Raman et al. (2012)
5,7-dihydroxy-4'-methoxy flavone	Acacetin	Suksamrarn et al. (2004)
5,7,3',4'-tetrahydroxy flavone	Luteolin	-
5-hydroxy-6,7,3',4'-tetramethoxy flavone	-	Phan et al. (2001)
5,7-dihydroxy-6,3',4'-trimethoxy flavone	Eupatilin	Phan et al. (2001)
Kaempferol-3-O-rutinoside	-	Ling et al. (2007)
Quercetin-3-O-rutinoside	-	Ling et al. (2007)
Taxifolin-4'-methyl ether	-	Ling et al. (2007) and Johari et al. (2012)
Aromadendrin-4'-methyl ether	-	Ling et al. (2007) and Johari et al. (2012)

**Table 3**  
Overview of reported antibacterial activities of different *Chromolaena odorata* (Asian/West African biotype) extracts.

Extract	Test model	Organism tested <sup>a</sup>	Result	MIC (mg/ml)	References
<b>Ethanol</b>	Agar diffusion	<i>Sa</i>	Sensitive	0.1	Anyasor et al. (2011)
		<i>Ec</i>	Sensitive	0.8	Anyasor et al. (2011)
		<i>Pa</i>	Resistant	Not stated	Anyasor et al. (2011)
		<i>St</i>	Sensitive	Not stated	Anyasor et al. (2011)
		<i>Pv</i>	Resistant	Not stated	Anyasor et al. (2011)
		<i>Kp</i>	Resistant	Not stated	Anyasor et al. (2011)
<b>Aqueous</b>	Agar diffusion	<i>Sa</i>	Sensitive	Not stated	Anyasor et al. (2011)
		<i>Ec</i>	Resistant	Not stated	Anyasor et al. (2011)
		<i>Pa</i>	Resistant	Not stated	Anyasor et al. (2011)
		<i>St</i>	Sensitive	Not stated	Anyasor et al. (2011)
		<i>Pv</i>	Resistant	Not stated	Anyasor et al. (2011)
		<i>Kp</i>	Resistant	Not stated	Anyasor et al. (2011)
<b>Methanol</b>	Agar diffusion	<i>Sa</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>Bs</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>Cg</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>St*</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>Ec</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>Kp</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>Pv</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>St</i>	Sensitive	0.01-1	Raman et al. (2012)
		<i>Vp</i>	Sensitive	0.01-1	Raman et al. (2012)
		<b>Aqueous</b>	Agar diffusion	<i>Sa</i>	Sensitive
<i>Bs</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>Cg</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>St</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>Ec</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>kp</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>Pv</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>St</i>	Sensitive			0.01-1	Raman et al. (2012)
<i>Vp</i>	Sensitive			0.01-1	Raman et al. (2012)
<b>Crude extract</b>	Agar diffusion			<i>St</i>	Sensitive
		<i>Ec</i>	Sensitive	Not stated	Zige et al. (2013)
<b>Ethanol</b>		<i>St</i>	Sensitive	Not stated	Zige et al. (2013)
		<i>Ec</i>	Sensitive	Not stated	Zige et al. (2013)
<b>Aqueous</b>		<i>St</i>	Sensitive	Not stated	Zige et al. (2013)
		<i>Ec</i>	Sensitive	Not stated	Zige et al. (2013)
<b>Cyclohexane</b>	Microdilution	<i>Ko</i>	Sensitive	1.25	Atindehou et al. (2013)
		<i>Se</i>	Sensitive	1.25	Atindehou et al. (2013)
		<i>Ss</i>	Sensitive	1.25	Atindehou et al. (2013)
		<i>Vc</i>	Sensitive	1.25	Atindehou et al. (2013)
<b>Dichloromethane</b>	Microdilution	<i>Ko</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Se</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Ss</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Vc</i>	Sensitive	0.156	Atindehou et al. (2013)
<b>Ethyl acetate</b>	Microdilution	<i>Ko</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Se</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Ss</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Vc</i>	Sensitive	0.625	Atindehou et al. (2013)
<b>Butanol</b>	Microdilution	<i>Ko</i>	Sensitive	1.25	Atindehou et al. (2013)
		<i>Se</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Ss</i>	Sensitive	0.625	Atindehou et al. (2013)
		<i>Vc</i>	Sensitive	0.312	Atindehou et al. (2013)
<b>Ethanol</b>	Agar diffusion	<i>Pa</i>	Sensitive	8.0	Irobi (1992)
		<i>Sf</i>	Sensitive	6.0	Irobi (1992)
<b>Ethyl acetate</b>	Microdilution	<i>Bs</i>	Sensitive	7.0	Naidoo et al. (2011)
		<i>Bc</i>	Sensitive	8.0	Naidoo et al. (2011)
		<i>Sa</i>	Sensitive	8.0	Naidoo et al. (2011)
		<i>Se*</i>	Sensitive	7.0	Naidoo et al. (2011)
		<i>Ec</i>	Resistant	No activity	Naidoo et al. (2011)
		<i>Pv</i>	Resistant	No activity	Naidoo et al. (2011)
		<i>Ss</i>	Resistant	No activity	Naidoo et al. (2011)
		<i>Ea</i>	Resistant	No activity	Naidoo et al. (2011)
		<b>Methanol</b>	Microdilution	<i>Bs</i>	Sensitive
<i>Bc</i>	Sensitive			7.5	Naidoo et al. (2011)
<i>Sa</i>	Sensitive			8.0	Naidoo et al. (2011)
<i>Se</i>	Sensitive			8.0	Naidoo et al. (2011)
<i>Ec</i>	Sensitive			8.5	Naidoo et al. (2011)
<i>Pv</i>	Resistant			No activity	Naidoo et al. (2011)

Table 3 (continued)

Extract	Test model	Organism tested <sup>a</sup>	Result	MIC (mg/ml)	References
Water	Microdilution	Ss	Resistant	No activity	Naidoo et al. (2011)
		Ea	Resistant	No activity	Naidoo et al. (2011)
		Bs	Resistant	No activity	Naidoo et al. (2011)
		Bc	Resistant	No activity	Naidoo et al. (2011)
		Sa	Resistant	No activity	Naidoo et al. (2011)
		Se	Resistant	No activity	Naidoo et al. (2011)
		Ec	Resistant	No activity	Naidoo et al. (2011)
		Pv	Resistant	No activity	Naidoo et al. (2011)
		Ss	Resistant	No activity	Naidoo et al. (2011)
		Ea	Resistant	No activity	Naidoo et al. (2011)

<sup>a</sup> Bc, *Bacillus cereus*; Bs, *Bacillus subtilis*; Cg, *Corynebacterium glutamicum*; Ea, *Enterobacter aerogenes*; Ec, *Escherichia coli*; Ko, *Klebsiella oxytoca*; Kp, *Klebsiella pneumoniae*; Pa, *Pseudomonas aeruginosa*; Pv, *Proteus vulgaris*; Sa, *Staphylococcus aureus*; Se, *Salmonella enterica*; Se\*, *Staphylococcus epidermidis*; Ss, *Shigella sonnei*; Sf, *Streptococcus faecalis*; St, *Salmonella typhi*; St\*, *Streptococcus thermophilus*; Ss, *Shigella sonnei*; Vc, *Vibrio cholerae*; Vp, *Vibrio parahaemolyticus*.

and a cadinol isomer. Pisutthanan et al. (2006) isolated transocimene, bulnesol,  $\delta$ -cadinene, geijerene, pregeijerene, germacrene D,  $\alpha$ -pinene,  $\beta$ -pinene,  $\beta$ -caryophyllene and vestitenone from the aerial parts of *C. odorata* in Thailand. Also,  $\alpha$ -pinene,  $\beta$ -pinene, geigerene, pregeijerene and germacrene D have been isolated from fresh leaves of *C. odorata* in Benin Republic (Avlessi et al., 2012). Lamaty et al. (1992) isolated p-cymene and  $\alpha$ -pinene from *C. odorata* collected from Congo and Cameroon. Joshi (2013a) isolated some essential oils from the aerial parts and flowers of *C. odorata* in India including khusimone,  $\alpha$ -muurolol, geijerene, pregeijerene, cyperene, germacrene D,  $\delta$ -cadinene, epi-cubebol, cubebol, cis-sabinene hydrate, 10-epi- $\gamma$ -eudesmol and germacrene-D-4-ol. The same study was carried out on the roots of *C. odorata*, and 4 essential oils were discovered which have not previously been reported in the species including himachalol, 7-isopropyl-1,4-dimethyl-2-azulenol, androencecalinol and 2-methoxy-6-(1-methoxy-2-propenyl) naphthalene (Joshi, 2013b). A pentacyclic triterpenoid (amyrin) has also been isolated from fresh leaves of *C. odorata* in India (Prabhu and Ravi, 2012).

3.2.2.3. Alkaloids and other natural products. *C. odorata* contains a number of pyrrolizidine alkaloids (PAs). Biller et al. (1994) isolated five N-oxide pyrrolizidine alkaloids which include 7-angeloylretronecine, 9-angeloylretronecine, 3'-acetylretronecine, intermedine and rinderine from the roots of *C. odorata*. *C. odorata* employs these alkaloids as defensive compounds against generalist phytophagous insects because of their toxicity (Macel, 2011). Although PAs can be hazardous to the health of humans and animals because of their toxicity, PA-containing plants are still in use in many traditional medicines in Africa (Roeder and Wiedenfeld, 2011). The various types of PAs have different potential for causing toxic reactions so more investigation is needed in this area concerning the toxicity of the compounds present in *C. odorata*. More than 350 PAs have been identified in over 6000 species in the Boraginaceae, Compositae (Asteraceae) and Leguminosae (Fabaceae) families and about half of the identified PAs are toxic (Stegelmeier et al., 1999).

Phytochemical studies on the extracts of *C. odorata* have indicated the presence of tannins, terpenoids, cardiac glycosides, saponins, anthraquinones (Akinmoladun et al., 2007; Panda et al., 2010; Anyasor et al., 2011; Vijayaraghavan et al., 2013), carbohydrates and proteins (Nwinuka et al., 2009). Data on specific compounds are however needed.

### 3.2.3. Bioactivities of *C. odorata*

3.2.3.1. Antibacterial activity. Reports have shown that *C. odorata* exhibited anti-bacterial activity against opportunistic human pathogens (Irobi, 1992; Caceres et al., 1995). Atindehou et al. (2013) tested cyclohexane, dichloromethane, ethyl acetate and butanol

extracts of *C. odorata* leaves for their antibacterial activity against four bacteria that cause intestinal tract infection, namely *Klebsiella oxytoca*, *Salmonella enterica*, *Shigella sonnei* and *Vibrio cholerae* isolated from patients confirmed to have diarrhoea in France. The display of anti-bacterial activity in terms of minimum inhibition concentration (MIC) values ranged from 0.15 to 1.2 mg/ml. The best activity was obtained against *V. cholerae* with MIC=0.15 mg/ml for the dichloromethane extract and MIC=0.31 mg/ml for the butanol extract. The MIC values indicate that *C. odorata* may be a good source of antibacterial compounds although it is generally accepted that an MIC value of below 0.1 mg/ml relates to good antimicrobial activity for a crude extract. The methanol extract from *C. odorata* inhibited the growth of clinical bacteria such as *Staphylococcus aureus* and *Escherichia coli* (Sukanya et al., 2011). Raman et al. (2012) tested ethanol, methanol, chloroform and a mixture of methanol:chloroform:water in the ratio 12:5:3 extracts of *C. odorata* leaves against nine strains of bacteria (*Bacillus subtilis*, *Corynebacterium glutamicum*, *E. coli*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Salmonella typhi*, *S. aureus*, *Streptococcus thermophilus* and *Vibrio parahaemolyticus*). The study was performed employing the agar well diffusion method, and inhibition zones were determined using the Himedia zone of inhibition scale. The MIC of the extracts was determined for all bacterial species using the two-fold serial microdilution method with saline, at final concentrations ranging from 0 to 200 mg/ml. The methanol (MIC: 0.14 mg/ml) and aqueous extracts (MIC: 0.162 mg/ml) showed the highest antibacterial activity against all tested bacteria. Anyasor et al. (2011) tested ethanolic and aqueous extracts of *C. odorata* leaves against *K. pneumoniae*, *S. aureus*, *E. coli*, *P. vulgaris* and *Pseudomonas aeruginosa*, using the agar diffusion method. The growth of *P. aeruginosa*, *P. vulgaris* and *K. pneumoniae* was not inhibited by any of the extracts. The highest inhibition zone was exhibited against *S. aureus* with a zone diameter of 14 mm at a concentration of 250 mg/ml ethanolic extract, with the lowest MIC of 0.1 mg/ml, while the lowest zone of growth of inhibition was 1 mm at 150 mg/ml concentration for the ethanolic extract on *E. coli*. The ethanolic extract at 250 mg/ml, 200 mg/ml and 150 mg/ml only showed minimum inhibition zones against *E. coli*. The highest MIC, and therefore weakest activity, was obtained against *E. coli* with MIC=0.8 mg/ml.

Water, ethyl acetate and methanol extracts of *C. odorata* were tested against four strains of Gram-positive bacteria (*B. subtilis*, *Bacillus cereus*, *S. aureus*, and *Staphylococcus epidermidis*) and four strains of Gram-negative bacteria (*E. coli*, *P. vulgaris*, *Enterobacter aerogenes* and *S. sonnei*). The methanol leaf extract was the most effective against the four Gram-positive bacteria as well as one Gram-negative species, *E. coli*. The growth of the other three Gram-negative bacteria was not inhibited by any of the extracts

(Naidoo et al., 2011). Zige et al. (2013) carried out an antimicrobial investigation against two bacteria, *S. typhi* and *E. coli*, of crude water and ethanol extracts of *C. odorata* leaves using the well diffusion method. About 1 mg/ml of each extract was introduced in each well. The three extracts were found to possess significant anti-bacterial activity against the tested bacterial pathogens. The highest inhibition zone (37.7 mm) for *S. typhi* was from the ethanol extract and *E. coli* (32.3 mm) from the aqueous extract. *P. aeruginosa* (Gram-negative) and *Streptococcus faecalis* (Gram-positive) were tested against the ethanol extract of the species using the agar dilution method. *P. aeruginosa* had a mean inhibition zone of 7 mm and MIC of 8.0 mg/ml, while for *S. faecalis* the mean inhibition zone of 12 mm and MIC of 6.0 mg/ml was reported (Irobi, 1992).

Clinically, a plant extract or compound is of little relevance if the MIC value is over 1 mg/ml but it can possess some inert substances that may show good anti-bacterial properties at higher concentrations (Gibbons, 2004). The minimum inhibition zones exhibited by extracts of *C. odorata* on Gram-positive bacteria and some Gram-negative bacteria suggests that the species has potential in health care delivery systems, serving as an alternative to orthodox antibiotics in the treatment of microbial infections, especially as these bacteria often develop resistance to known antibiotics (Singleton, 1999). Efflux inhibitory activity of flavonoid compounds extracted from *C. odorata* against selected methicillin-resistant *S. aureus* isolates also suggest that the plant is a good efflux inhibitor (Johari et al., 2012).

Recent studies have demonstrated the resistance of various species of bacteria to antibiotics. For example, Younes et al. (2011) reported resistance of *K. oxytoca* isolated from Scottish patients to ceftazidime and cefotaxime due to the expression of cefotaximase by the bacteria. Also in the United States, the resistance of *S. enterica* to ciprofloxacin in the last decade has been reported (Meddalla et al., 2011). *V. cholerae* has been found to be resistant to some antibiotics (Alaoui et al., 2010). Several strains of *Shigella* have displayed resistance to trimetoprine-sulfamethazole and tetracycline. Research carried out in China showed resistance of *Shigella* to multiple antibiotics such as aztreonam (30.8%), ampicillin (92.3%), gentamicin (53.8%), piperacillin (61.5%), ceftazidime (30.8%), cefotaxime (30.8%) and ampicillin (92.3%). The screening of medicinal plants such as *C. odorata* for new bioactive agents against bacteria is promising as the species is effective against some bacteria such as *S. faecalis*, *P. aeruginosa* (Irobi, 1992), *S. typhi* and *E. coli* (Zige et al., 2013), *B. subtilis*, *B. cereus*, *S. aureus*, *S. epidermidis* and *E. coli* (Naidoo et al., 2011; Sukanya et al., 2011) as well as *V. cholerae* (Atindehou et al., 2013).

**3.2.3.2. Anti-inflammatory activity.** The anti-inflammatory activities of aqueous (Owoyele et al., 2005) and ethanolic (Owoyele et al., 2006) extracts of *C. odorata* were investigated on rats in three inflammatory models; carrageenan, cotton pellet and formalin (arthritis), representing acute and chronic forms of inflammation. The aqueous and ethanolic extracts at a minimum concentration of 25 mg/kg produced significant inhibition (69.6%, 63.9%) of carrageenan-induced oedema after 5 h of carrageenan administration, and higher doses of 200 mg/kg inhibited carrageenan-induced oedema to 95.0 and 94.4%. In the cotton pellet-induced granuloma assay, the aqueous and ethanolic extracts significantly reduced the weight of the granuloma at the minimum dose of 25 mg/kg (14.3%, 7.1%) and a higher dose of 200 mg/kg (35.7%, 28.8%). The growth of paw oedema was also significantly reduced at doses from 25 to 200 mg/kg in the formalin-induced arthritis test. Based on these results, *C. odorata* seems to have good anti-inflammatory activity, probably because of the presence of phenolic compounds.

**3.2.3.3. Analgesic and anti-immunosuppressive activity.** Owoyele et al. (2006) documented the analgesic activities of ethanolic extracts of *C. odorata* applied at doses of 25–200 mg/kg using various assays. In the hot plate latency assay, doses of 25–200 mg/kg of the ethanolic extract were administered to rats after which they were placed on a hot plate at 55 °C. At doses of 100 and 200 mg/kg, there were significant increases in the reaction time from  $1.80 \pm 0.37$  to  $4.0 \pm 0.55$  min after 60 min of administration. In the formalin-induced paw licking assay, the ethanolic extract at doses of 25–200 mg/kg significantly inhibited the early and late phase. At a minimum dose of 25 mg/kg, the early phase and late phase times of inhibition were  $131.6 \pm 5.8$  and  $89.6 \pm 5.8$  min respectively; at a higher dose of 200 mg/kg, the early and late phase times of inhibition were  $52.8 \pm 4.6$  and  $26.2 \pm 2.4$  min respectively. The number of writhing incidents was significantly decreased from  $16.0 \pm 0.37$  to  $7.0 \pm 0.26$  at doses between 25 and 200 mg/kg extract administration in the acetic acid induced writhing test.

Research carried out on the ethanolic extract of *C. odorata* leaves (Nudo et al., 2012) showed that the plant has the potential to reverse drug-induced immunosuppression, a common consequence of long-term use of cyclophosphamide (Cy) therapy in cancer patients (Bin-Hafeez et al., 2001). This drug is known to cause leucopenia as it is cytotoxic, not only to cancer cells but to leucocytes as well.

**3.2.3.4. Antioxidant activity.** Raman et al. (2012) tested the methanol extract of *C. odorata* for its antioxidant capacity using the DPPH radical scavenging method. The methanol extract was able to react with the stable free radical 2, 2'-diphenyl-1-picrylhydrazyl by converting it to 1,1-diphenyl-2-picryl hydrazine at a concentration of 10.2 µg/ml. In comparing different solvent extracts of *C. odorata*, Vijayaraghavan et al. (2013) tested methanol, ethanol, petroleum ether, chloroform and aqueous extracts of *C. odorata* leaves for free radical scavenging activity using the DPPH assay. The ethanolic leaf extract yielded the most effective DPPH radical scavenging activity at 94.29%. Rapid thin layer chromatographic screening for antioxidant activity was carried out by spotting concentrated ethanol and aqueous solutions of *C. odorata* leaves on silica gel plates. The rapid TLC screening was positive for extracts, showing IC<sub>50</sub> (half maximum inhibitory concentration) values of 22.50 µg for the aqueous extract and 23.70 µg for the ethanolic extract.

*In vitro* antioxidant activity of the ethanolic extract of *C. odorata* was carried out by Parameswari and Suriyavathana (2012) using different free radical scavenging assays: DPPH, superoxide, reducing power, nitric oxide, FRAP, ABTS, chelating ability and hydroxyl radical scavenging activity. At 200–1000 µg, the antioxidant activity of the ethanolic extract was 24.68–61.78%. At 200–1000 µg the superoxide scavenging activity was 19.42–56.12%. In the reducing power activity, the extract showed increased absorbance with increased concentrations ranging from 200 µg to 1000 µg. The minimum percentage scavenging activity at 200 µg was 28.78% and the maximum at 1000 µg was 64.68% for nitric oxide scavenging activity. The ferric ability (FRAP) of the extract at 200–1000 µg was in the range of 0.07–0.17. ABTS scavenging activity of the ethanolic extract at concentrations from 200 µg to 1000 µg were 29.92–63.34%. The ethanolic extract minimum chelating ability was 20.68% at 200 µg while the maximum ability was 71.96% at 1000 µg. *C. odorata* leaf extract exhibited a minimum activity of 29.78% at 200 µg, and maximum activity of 64.14% at 1000 µg. Due to the high amounts of polyphenols, *C. odorata* seems to be a rich source of natural antioxidants.

**3.2.3.5. Cytotoxic activity.** Prabhu and Ravi (2012) investigated the *in vitro* cytotoxic activity of a triterpene suspected to be amyirin extracted from fresh leaves of *C. odorata* against a hepatocellular



carcinoma (HepG2) cell line, using the MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide] assay. The triterpene showed cytotoxic effects on the HepG2 cancer cell line in a dose dependent pattern and the IC<sub>50</sub> was determined to be 206.7 µg/ml. With HepG2 cells exposed to concentrations below 206 µg/ml, there was no activity observed but at 206 µg/ml, 90% inhibition was observed. Further studies on these aspects are needed to establish if *C. odorata* will be a good source of anticancer drugs.

**3.2.3.6. Antifungal activity.** Leaf and stem aqueous and ethanolic extracts of *C. odorata* were screened for antifungal activity against *Aspergillus flavus*, *Aspergillus glaucus*, *Candida albicans*, *Candida tropicalis* and *Trichophyton rubrum* by Naidoo et al. (2011) in South Africa. The ethanolic extract of *C. odorata* showed more antifungal activity than the aqueous leaf and stem extracts. The leaf ethanolic extract was more effective than the stem extract. The extracts only displayed good antifungal activity at higher concentrations. In Cameroon, the aqueous ethanol extract of *C. odorata* was also found to be sensitive against *Cryptococcus neoformans*, *Microsporium gypseum*, *T. rubrum* and *Trichophyton mentagrophytes* (Ngonu et al., 2006).

**3.2.3.7. Anthelmintic activity.** Panda et al. (2010) investigated the anthelmintic activity of petroleum ether, ethyl acetate and methanol extracts of *C. odorata* against earthworms, using piperazine citrate and albendazole drugs as references. Though all extracts showed activity, the methanol extract was most effective. The extracts were found to be lethal to the worms at 10 mg/ml of the petroleum ether extract and at 5 mg/ml concentrations of ethyl acetate and methanol extracts. Paralysis occurred at 5 mg/ml with all the extracts. The effectiveness of these extracts was comparable to albendazole and piperazine citrate used as reference drugs. The above information shows that *C. odorata* may be a promising source of anthelmintic drugs, though more research will be necessary to further confirm this activity.

**3.2.3.8. Haemostatic and wound healing activity.** Pandith et al. (2012) carried out *in vivo* and *in vitro* haemostatic activity tests on fresh leaf lyophilised aqueous and 70% ethanol extracts and 50, 70 and 95% dried ethanol leaf extracts of *C. odorata*. Though all extracts displayed significant reduction in bleeding time (< 2.5 min), the 70% dried leaf ethanolic extract showed the highest percentage transmission by producing the highest haemostatic activity *in vivo* with the shortest bleeding time of 1.85 min. All extracts did not induce platelet aggregation or blood clotting in the *in vitro* study.

Panda et al. (2010) carried out an investigation on the wound healing potential of *C. odorata* using the excision wound model test, by testing the effectiveness of petroleum ether, ethyl acetate and methanol extracts of the plant in rats compared with Neosporin (Burroughs Wellcome Inc.) and Betadine (Win Medicare) ointments as reference standards. The extract solutions (5, 7.5 and 10%) w/w at a quantity of 0.5 g each, and a simple solvent base, with Neosporin and Betadine applied in similar quantities as the control and standard respectively, were used to monitor the wound healing potential by wound contraction and wound closure time. Although the petroleum ether and ethyl acetate extracts showed significant activity, the methanolic extract of *C. odorata* was most effective. The wound healing activity was dependent on the concentrations of the different extracts and potency of the extracts was inversely proportional to the time taken for healing. The effectiveness of the extracts was comparable with Neosporin and Betadine. Ethanolic and aqueous extracts of *C. odorata* were also tested for wound healing potential (Anyasor et al., 2011) using normal saline as a control. In the aqueous extract the lowest time of clotting was 0.26 ± 0.012 min, ethanol 2.03 ± 0.035 min and normal saline 6.88 ± 0.007 min which was the longest clotting

time. In the coagulation test also carried out, the aqueous extract showed the lowest coagulation time, 15.18 ± 0.023 min, with the ethanolic extract values 21.78 ± 0.696 min and control values 162.28 ± 17.371 min.

Phan et al. (2001) carried out an investigation on the anti-oxidant effects of the ethanolic and polyphenolic extracts from the leaves of *C. odorata* on human dermal fibroblasts and epidermal keratinocytes against hydrogen peroxide and hypoxanthine-xanthine oxidase-induced damage using the MTT assay. For fibroblasts, toxicity of hydrogen peroxide or hypoxanthine-xanthine oxidase on cells was dose-dependent. The total ethanol extract at a concentration of 50 µg/ml had slightly protective effects on fibroblasts against hydrogen peroxide and hypoxanthine-xanthine oxidase-induced damage, while at 400 and 800 µg/ml the extract showed maximum and consistent protective cellular effects on oxidant toxicity at low or high doses of oxidants. For keratinocytes, a dose-dependent relationship of oxidant toxicity was only seen with hydrogen peroxide but the protective action of the extract correlated with oxidant dosage. The total ethanol extract at 400 µg/ml and 800 µg/ml showed dose-dependent effects with both low and high concentrations of oxidants, while at 50 µg/ml the extract had no effect on keratinocytes. The polyphenolic extract only exhibited a slight antioxidant effect.

In another experiment, isolated phenolic compounds from *C. odorata* were investigated for protective effects against oxidative damage of cultured skin cells by Phan et al. (2001) using colorimetric and lactate dehydrogenase (LDH) release assays. The results showed that the phenolic acids present and complex mixtures of lipophilic flavonoid aglycones protect cultured skin cells against oxidative damage. These results show that *C. odorata* is an important species because of the vital role it plays to arrest bleeding and in treating burns and wounds. Protection of cells against destruction in wound healing, which provides justification for its wide use in traditional medicine preparations as inflammatory mediators may be one of the ways in which the extracts from *C. odorata* contribute to the wound healing process (Phan et al., 2001). Eupolin, a product from *C. odorata* leaves for treating soft tissue burns and wounds, has been licensed for use in Vietnam (Phan et al., 1998; Raina et al., 2008). This important property possessed by the species is believed to occur as a result of saponins and tannins, essential oils and phenolic compounds present in the plant.

**3.2.3.9. Other activities.** *C. odorata* has been reported to possess anti-pyretic, antispasmodic (Taiwo et al., 2000) and anti-malarial (Ongkana, 2003) activities, but additional detailed investigations are yet to be carried out. Amazu et al. (2013) carried out a study on anticonvulsant activity of aqueous and ethanolic extracts of *C. odorata* in rats at doses of 25–100 mg/kg with valproic acid at 200 mg/kg as the standard. The extracts exhibited a dose dependent anticonvulsant activity. At doses of 25–50 mg/kg the activity was comparable with valproic acid while at 100 mg/kg the activity was higher than that of valproic acid. This activity may be as a result of the presence of alkaloids, flavonoids and kauronic acid that have been discovered in this species. Kauronic acid, which was originally isolated from honey bees, has now been found to be present in *C. odorata* (Wafo et al., 2012). The compound has good anticonvulsant potential and is effective against epileptogenesis. The species has also been reported to have fungicidal and nematocidal properties (Ilondu, 2011; Odeyemi et al., 2011).

### 3.2.4. Toxicological data

*C. odorata* contains pyrrolizidine alkaloids (PAs) which may be poisonous to grazing animals such as cattle and goats (Sajise, et al., 1974; McFadyen, 2004). Pyrrolizidine alkaloids have been shown to exhibit a large variety of genotoxic effects including DNA

binding and DNA cross-linking, chromosomal aberrations, mutagenicity and carcinogenicity (Mattocks, 1986; Petry et al., 1986; Kim et al., 1999). As PAs can be hazardous to the health of humans and animals because of their toxicity (Roeder and Wiedenfeld, 2011), it is important to clinically investigate the dosage range that is safe for humans in treating various diseases.

#### 4. Conclusions

The analysis and synthesis of literature on *C. odorata* shows that the species has spread to several countries in West, Central, East and southern Africa (Zachariades et al., 2009; 2013). The southern African biotype of *C. odorata* which originated from Cuba or Jamaica has been shown to be morphologically and genetically distinct from the more widespread biotype (Asian/West African biotype) invading Asia, Oceania, East, Central and West Africa (Paterson and Zachariades, 2013). In its invasive range, *C. odorata* grows in a wide range of vegetation types such as forest margins, grasslands, roadsides, agricultural lands and disturbed forests (Zachariades et al., 2009; Uyi and Igbinosa, 2013). As is common with other invasive plant species, *C. odorata* impacts negatively on agriculture, livelihoods and biodiversity conservation causing significant economic losses (Lucas, 1989; Zachariades et al., 2009; Uyi et al., 2014 and references therein).

Regardless of the negative impacts of *C. odorata*, it has been found useful in the field of traditional medicinal practice. Its use as a fallow plant and as a soil fertility improvement plant in the slash and burn rotation system for agriculture is increasingly recognised in some sub-Saharan African countries. Its use in traditional medicine has prompted many researchers to carry out various investigations on the medicinal potential of the plant. Phenolic compounds present in *C. odorata* are largely responsible for the antioxidant properties possessed by the plant and some other bioactivities, and they are good radical scavengers. Free radicals are one of the causes of several diseases such as Alzheimer's-type dementia and Parkinson's disease, and *C. odorata* may be a promising candidate against these diseases as it contains high levels of phenolic compounds which are capable of inhibiting or quenching free radicals, terminating the free radical chain reaction and acting as reducing agents.

The cytotoxic, antibacterial, antifungal, haemostatic/wound healing and antioxidant potential of *C. odorata* discussed in this paper shows that the plant is worthy of further investigation, especially the dose ranges that should be applied in respect to various ailments. Apart from the study carried out by Naidoo et al. (2011) on the SAB, every other investigation reported in this paper has been undertaken on the AWAB. Whether the SAB also possesses all the properties and contains the same secondary metabolite compounds that have been isolated from the AWAB remains to be seen. Further studies on the phytochemistry and pharmacological properties on the SAB biotype will not only further our knowledge of ethnobotany and ethnomedicine, but could also create awareness on its medicinal use, thereby improving the health and knowledge of local people.

#### Conflict of interest

The authors of this review paper declare no conflict of interest.

#### Acknowledgement

The University of KwaZulu-Natal, South Africa is highly appreciated for providing research facilities and funding.

#### References

- Adjanohoun, E., Ake-Assi, L., 1979. Contribution au Recensement des Plantes Médicinales de Côte d'Ivoire. Centre National de Floristique, Abidjan, Ivory Coast.
- Agunbiade, F.O., Fawale, A.T., 2009. Use of siam weed biomarker in assessing heavy metal contaminations in traffic and solid waste polluted areas. *Int. J. Environ. Sci. Technol.* 6, 267–276.
- Akinmoladun, A.C., Ibukun, E.O., Dan-Ologe, I.A., 2007. Phytochemical constituents and antioxidant properties of extracts from the leaves of *Chromolaena odorata*. *Sci. Res. Essays* 2, 191–194.
- Akobundu, I.O., Ekeleme, F., Chikoye, D., 1999. Influence of fallow management systems and frequency of cropping on weed growth and crop yield. *Weed Res.* 39, 241–256.
- Alaoui, H.L., Oufdou, K., Mezrioui, N.E., 2010. Determination of several potential virulence factors in non-ol *Vibrio cholera*, *Pseudomonas aeruginosa*, faecal coliforms and Streptococci isolated from Marrakesh ground water. *Water Sci. Technol.* 61, 1895–1905.
- Alcantara, H.J.P., Rivero, G.C., Puzon, J.M., 2013. Tolerance mechanisms in mercury exposed *Chromolaena odorata* (L.f) R.M. King and H. Robinson, a potential phytoremediator. *J. Degrad. Min. Lands Manag.* 1, 9–20.
- Amatya, S., Tuladhar, S.M., 2011. *In vitro* antioxidant activity of extracts from *Eupatorium odoratum* L. *Res. J. Med. Plant* 5, 79–84.
- Amazu, L.U., Omoregie, P., Ajugwo, A.O., Ifezulike, C.C., Azikiwe, C.C.A., 2013. Anticonvulsant potency of the leaf extract of *Chromolaena odorata* in rats. *Unique Res. J. Med. Med. Sci.* 1, 64–69.
- Anoliefo, G.O., Vwioko, D.E., Mpamah, P., 2003. Regeneration of *Chromolaena odorata* (L.) K. & R. in crude oil polluted soil: a possible phytoremediating agent. *Benin Sci. Dig.* 1, 9–16.
- Anyasor, G.N., Aina, D.A., Olushola, M., Aniyikawe, A.F., 2011. Phytochemical constituents, proximate analysis, antioxidants, anti-bacterial and wound healing properties of leaf extracts of *Chromolaena odorata*. *Ann. Biol. Res.* 2, 441–451.
- Apori, S.O., Long, R.J., Castro, F.B., Erskov, E.R., 2000. Chemical composition and nutritive value of leaves and stems of tropical weed *Chromolaena odorata*. *Grass Forage Sci.* 55, 77–81.
- Atindehou, M., Lagnika, L., Guérol, B., Strub, Jean Marc, Zhao, J.M., Dorsselaer, M., Marchioni, A.V., Prévost, E., Haikel, G., Taddéi, Y., Sanni, C., Metz-Boutigue, M., A., 2013. Isolation and identification of two anti-bacterial agents from *Chromolaena odorata* L. active against four diarrheal strains. *Adv. Microbiol.* 3, 115–121.
- Avlessi, F., Alitonou, G.A., Djenontin, T.S., Tchobo, F., Yehouenou, B., Menut, C., Sohouhoulou, D., 2012. Chemical composition and biological activities of the essential oil extracted from the fresh leaves of *Chromolaena odorata* (L. Robinson) growing in Benin. *ISCA J. Biol. Sci.* 1, 7–13.
- Ayensu, E.S., 1978. Medicinal Plants of West Africa. Reference Publication Inc. Algonac, Michigan, USA.
- Barua, R.N., Sharma, R.P., Thyagarajan, G., Herz, W., 1978. Flavonoids of *Chromolaena odorata*. *Phytochemistry* 17, 1807–1808.
- Bhargava, D., Sanjay, K., Jagadish, N.S., Bicash, S., Chiranjit, M.S., 2011. Screening of anti-gonorrhoeal activity of some medicinal plants in Nepal. *Int. J. Pharmacol. Biosci.* 2, 203–212.
- Billar, A., Boppré, M., Witte, L., Hartmann, T., 1994. Pyrrolizidine alkaloids in *Chromolaena odorata*. Chemical and chemoeological aspects. *Phytochemistry* 35, 615–619.
- Bin-Hafeez, B., Ahmad, I., Haque, R., Raisuddin, S., 2001. Protective effect of *Cassia occidentalis* L. on cyclophosphamide-induced suppression of humoral immunity in mice. *J. Ethnopharmacol.* 75, 13–18.
- Caceres, A., Menendez, H., Mendez, E., Cohobon, E., Samayoa, B.E., Jauregui, E., Peralta, E., Carrillo, G., 1995. Anti-gonorrhoeal activity of plants used in Guatemala for the treatment of sexually transmitted diseases. *J. Ethnopharmacol.* 48, 85–88.
- Chakraborty, A.K., Rambhade, S., Patil, U.K., 2011. *Chromolaena odorata* (L.): an overview. *J. Pharm. Res.* 4, 573–576.
- Gautier, L., 1992. Taxonomy and distribution of a tropical weed, *Chromolaena odorata* (L.) R. King and H. Robinson. *Candollea* 47, 645–662.
- Gibbons, S., 2004. Anti-staphylococcal plant natural products. *Nat. Prod. Rep.* 21, 263–277.
- Gill, L.S., 1992. Ethnomedical Uses of Plants. Nigeria. Uniben Press, Benin City, Nigeria.
- Goodall, J.M., Erasmus, D.J., 1996. Review of the status and the integrated control of the invasive weed, *Chromolaena odorata* in South Africa. *Agric. Ecosyst. Environ.* 56, 151–164.
- Hoovers, R., M'boob, S.S., 1996. The status of *Chromolaena odorata* (L.) R. M. King and H. Robinson in West and Central Africa. In: Prasad, U.K., Muniappan, R., Ferrar, P., Aeschliman, J.P., de Foresta, H. (Eds.), Proceedings of the Third International Workshop on Biological Control and Management of *Chromolaena odorata*. Publication 202. Agricultural Experiment Station, University of Guam, USA, Mangilao, Guam, pp. 1–5.
- Idu, M., Onyibe, H.I., 2007. Medicinal plants of Edo state, Nigeria. *Res. J. Med. Plant* 1, 32–41.
- Ilodu, E.M., 2011. Evaluation of some aqueous plant extracts used in the control of pawpaw fruit (*Carica papaya* L.) rot fungi. *J. Appl. Biosci.* 37, 2419–2424.
- Inya-Agha, S.I., Oguntimein, B.O., Sofowora, A., Benjamin, T.V., 1987. Phytochemical and anti-bacterial studies on the essential oil of *Eupatorium odoratum*. *Int. J. Crude Drug Res.* 25, 49–52.
- Irobi, O.N., 1992. Activities of *Chromolaena odorata* (Compositae) leaf extract against

- Pseudomonas aeruginosa* and *Streptococcus faecalis*. J. Ethnopharmacol. 37, 81–83.
- Ivens, G.W., 1974. The problem of *Eupatorium odoratum* L. in Nigeria. Pest Artic. News Summ. 20, 76–82.
- Iwu, M.M., Chiori, C.O., 1984. Antimicrobial activity of *Eupatorium odoratum* extract. Fitoterapia 55, 354–356.
- Jagadeesh, K.S., Geeta, G.S., Reddy, T.K.R., 1990. Biogas production by anaerobic digestion of *Eupatorium odoratum* L. Biol. Wastes 33, 67–70.
- Johari, S.A., Kiong, L.S., Mohtar, M., Isa, M.M., Man, S., Mustafa, S., Ali, A.M., 2012. Efflux inhibitory activity of flavonoids from *Chromolaena odorata* against selected methicillin-resistant *Staphylococcus aureus* (MRSA) isolates. Afr. J. Microbiol. Res. 6, 5631–5635.
- Joshi, R.K., 2013a. Chemical composition of the essential oils of aerial parts and flowers of *Chromolaena odorata* (L.) R.M. King & H. Rob. from Western Ghats region of North West Karnataka, India. J. Essent. Oil Bear. Plants 16, 71–75.
- Joshi, R.K., 2013b. Chemical composition of the essential oil of *Chromolaena odorata* (L.) R.M. King and H. Rob. roots from India. J. Chem. 2013, 1–4.
- Kim, H.Y., Stermitz, F.R., Li, J.K., Coulombe, R.A., 1999. Comparative DNA cross linking by activated pyrrolizidine alkaloids. Food Chem. Toxicol. 37, 619–625.
- Koutika, L.S., Rainey, H.J., 2010. *Chromolaena odorata* in different ecosystems: weed or a fallow plant. Appl. Ecol. Environ. Res. 8, 131–142.
- Kouamé, P.B., Jacques, C., Bedi, G., Silvestre, V., Loquet, D., Barillé Nion, S., Robins, R. J., Illa Tea, I., 2013. Phytochemicals isolated from leaves of *Chromolaena odorata*: impact on viability and clonogenicity of cancer cell lines. Phytother. Res. 27, 835–840.
- Lamaty, G., Menut, C., Amvam Zollo, P.H., Kuate, J.R., Bessiere, J.M., Ouamba, J.M., Silou, T., 1992. Aromatic plants of tropical Central Africa IV. Essential oil of *Eupatorium odoratum* L. from Cameroon and Congo. J. Essent. Oil Res. 4, 101–105.
- Lima, O.A., Polonsky, J., 1973. Flavonoid constituents of *Cephalanthus spatheliferus*. Phytochemistry 12, 913–916.
- Ling, S.K., Abdul Rashid, A., Salbiah, M., Siti, Asha, A.B., Mazura, M.P., Khoo, M.G.H., Vimala, S., Ong, B.K., Mastura, M., Nor Azah, M.A., 2007. Extraction and simultaneous detection of flavonoids in the leaves of *Chromolaena odorata* by RP-HPLC with DAD. In: Nik Zanariah, N.M., Sarifah, K.A., Nor Azman, H. (Eds.), Highlights of FRIM's IRPA Projects 2006: Identifying Potential Commercial Collaborators Project Evaluation Meeting. 14–15 Dec 2006. Forest Research Institute Malaysia, pp. 32–37.
- Lucas, E.O., 1989. Siam weed (*Chromolaena odorata*) and crop production in Nigeria. Outlook Agric. 18, 133–138.
- Macel, M., 2011. Attract and deter: a dual role for pyrrolizidine alkaloids in plant-insect interactions. Phytochem. Rev. 10, 75–82.
- Mattocks, A.R., 1986. Chemistry and Toxicology of Pyrrolizidine Alkaloids. Academic Press, London.
- McFadyen, R.E.C., 1989. Siam weed: a new threat to Australia's north. Plant Prot. Q. 4, 3–7.
- McFadyen, R.E.C., 2004. *Chromolaena* in East Timor: history, extent and control. In: Day, M.D., McFadyen, R.E. (Eds.), Proceedings of the Sixth International Workshop on Biological Control and Management of *Chromolaena odorata* ACIAR Technical Reports 55. ACIAR Publications, Canberra, Australia, pp. 8–10.
- Medalla, F., Sjolund-Karlsson, M., Shin, S., Harvey, E., Joyce, K., Theobald, L., Nygren, B.N., Pecic, G., Gay, K., Austin, J., Stuart, A., Blanton, E., Mintz, E.D., Whitchard, J. M., Barzilay, E.J., 2011. Ciprofloxacin-resistant *Salmonella enterica* Serotype Typhi, United States, 1999–2008. Emerg. Infectious Dis. 17, 1095–1098.
- Merfort, I., 1985. Flavonoide aus *Arnica montana* und *Arnica chamissonis*. Planta Med. 51, 136–138.
- Moni, N.S., Subramoniam, R., 1960. Essential oil from *Eupatorium odoratum* – a common weed in Kerala. Indian For. 86, 209.
- Morton, J.F., 1981. Atlas of Medicinal Plants of Middle America vol. 2. Charles C. Thomas, Springfield, USA.
- Naidoo, K.K., Cooposamy, R.M., Naidoo, G., 2011. Screening of *Chromolaena odorata* (L.) King and Robinson for anti-bacterial and anti-fungal properties. J. Med. Plant Res. 5, 4859–4862.
- Nel, J.L., Richardson, D.M., Rouget, M., Mgidi, T., Mzeke, N., Le Maitre, D.C., Van Wilgen, B.W., Schonegevel, L., Henderson, L., Naser, S., 2004. A proposed classification of invasive alien plant species in South Africa: towards prioritizing species and areas for management action. S. Afr. J. Sci. 100, 53–64.
- Ngono, N.A., Ebelle, E.R., Ndifor, F., Biyiti, L., Amvam, Z.P.H., Bouchet, P., 2006. Anti-fungal activity of *Chromolaena odorata* (L.) King & Robinson (Asteraceae) of Cameroon. Chemotherapy 52, 103–106.
- Nudo, L.P., Elena, S., Catap, P.H.D., 2012. Anti-immunosuppressive effect of *Chromolaena odorata* (L.) King & Robinson (Asteraceae) leaf extract in cyclophosphamide-injected balb/c mice. Philipp. J. Sci. 141, 35–43.
- Nur Jannah, M.H., Mahmood, A.A., Sidik, K., Salmah, I., 2006. Cytoprotective effects of honey in combination with aqueous and ethanol extracts from *Chromolaena odorata* L. (*Eupatorium odoratum*) in rats. J. Univ. Malays. Med. Cent. 9, 7–13.
- Nwinuka, N., Nwilo, B., Eresama, J., 2009. Nutritional and potential medicinal value of *Chromolaena odorata* leaves. Int. J. Trop. Agric. Food Syst. 3, 122–129.
- Odeyemi, I.S., Olalekan, F.Y., Sosanya, O.S., 2011. Effect of organic fertilizer and *Chromolaena odorata* residue on the pathogenicity of *Meloidogyne incognita* on maize. Arch. Phytopathol. Plant Prot. 44, 1046–1052.
- Ongkana, R., 2003. Phytochemistry and anti-malarial activity of *Eupatorium odoratum* (L.). Thesis submitted to Mahidol University, Bangkok, Thailand.
- Owolabi, M.S., Ogundajo, A., Yusuf, K.O., Lajide, L., Villanueva, H.E., Tuten, J.A., Setzer, W.N., 2010. Chemical composition and bioactivity of the essential oil of *Chromolaena odorata* from Nigeria. Rec. Nat. Prod. 4, 72–78.
- Owoyele, V.B., Adediji, J.O., Soladoye, A.O., 2005. Anti-inflammatory activity of aqueous leaf extract of *Chromolaena odorata*. Inflammopharmacology 13, 479–484.
- Owoyele, V.B., Soladoye, A.O., Panda, D., Dash, K.S., Dash, K.G., 2006. Anti-inflammatory and analgesic activities of ethanolic extract of *Chromolaena odorata* leaves. Chron. Common Dis. 18, 397–406.
- Panda, D., Dash, K.S., Dash, K.G., 2010. Qualitative phytochemical analysis and investigation of anthelmintic and wound healing potentials of various extracts of *Chromolaena odorata* LINN. collected from the locality of Mohuda Village, Berhampur (South Orissa). Int. J. Pharm. Sci. Rev. Res. 1, 122–126.
- Pandith, H., Thongpraditchoe, S., Wongkrajang, Y., Gritsanapan, W., 2012. *In vivo* and *in vitro* hemostatic activity of *Chromolaena odorata* leaf extract. Pharm. Biol. 50, 1073–1077.
- Parameswari, G., Suriyavathana, M., 2012. *In vitro* anti-oxidant activity of *Chromolaena odorata* (L.) King and Robinson. Int. Res. J. Pharm. 3, 187–192.
- Paterson, I.D., Zachariades, C., 2013. ISSRs indicate that *Chromolaena odorata* invading southern Africa originates in Jamaica or Cuba. Biol. Control 66, 132–139.
- Petry, T.W., Bowden, G.T., Buhler, D.R., Sipes, I.G., Sipes, K.G., 1986. Genotoxicity of the pyrrolizidine alkaloid jacobine in rats. Toxicol. Lett. 32, 275–281.
- Phan, T.T., Hughes, M.A., Cherry, G.W., 1998. Enhanced proliferation of fibroblasts and endothelial cells treated with an extract of the leaves of *Chromolaena odorata* (Eupolin), a herbal remedy for treating wounds. Plast. Reconstr. Surg. 101, 756–765.
- Phan, T.T., Wang, P., See, R.J., Grayer, S.Y., Chan, S.T., 2001. Phenolic compounds of *Chromolaena odorata* protect cultured skin cells from oxidative damage: implication for cutaneous wound healing. Biol. Pharm. Bull. 24, 1373–1379.
- Pisutthanon, N., Liawruangrath, B., Liawruangrath, S., Bremner, J.B., 2006. A new flavonoid from *Chromolaena odorata*. Nat. Prod. Res. 20, 1192–1198.
- Prabhu, V., Ravi, S., 2012. Isolation of a novel triterpene from the essential oil of fresh leaves of *Chromolaena odorata* and its *in vitro* cytotoxic activity against HepG2 cancer cell line. J. Appl. Pharm. Sci. 2, 132–136.
- Raina, R., Prawez, S., Verma, P.K., Pankaj, N.K., 2008. Medicinal plants and their role in wound healing. Outl. Vet. J. 3, 1–7.
- Raman, V.B., Samuel, L.A., Saradhi, P.M., Rao, N.B., Vamsi Krishna, N.A., Sudhakar, M., Radhakrishnan, T.M., 2012. Anti-bacterial, antioxidant activity and GC-MS analysis of *Eupatorium odoratum*. Asian J. Pharmacol. Clin. Res. 5, 99–106.
- Rambuda, T.D., Johnson, S.D., 2004. Breeding systems of invasive alien plants in South Africa: does Baker's rule apply? Divers. Distrib. 10, 409–416.
- Roeder, E., Wiedenfeld, H., 2011. Pyrrolizidine alkaloids in plants used in the traditional medicine of Madagascar and the Mascarene islands. Pharmazie 66, 637–647.
- Sajise, P.E., Palis, R.K., Norcio, N.V., Lales, J.S., 1974. The biology of *Chromolaena odorata* (L.) R. M. King and H. Robinson. flowering behaviour, pattern of growth and nitrate metabolism. Philipp. Weed Sci. Bull. 1, 17–24.
- Seibert, T.F., 1989. Biological control of the weed, *Chromolaena odorata* (Asteraceae), by *Pareuchaetes pseudoinsulata* (Lepidoptera: Arctiidae) on Guam and the Northern Mariana Islands. Entomophaga 35, 531–539.
- Singleton, P., 1999. Bacteria in Biology. Biotechnology and Medicine, 4th edition. John Wiley and Sons Ltd., New York.
- Sofowora, E.A., 1982. Medicinal plants and traditional medicine in Africa. John Wiley and Sons Ltd., New York, p. 432.
- Stegemeier, B.L., Edgar, J.A., Colegate, S.M., Gardner, D.R., Schoch, T.K., Coulombe, R. A., Molyneux, R.J., 1999. Pyrrolizidine alkaloid plants, metabolism and toxicity. J. Nat. Toxins 8, 95–116.
- Sukanya, S.L., Sudisha, J., Prakash, H.S., Fathima, S.K., 2011. Isolation and characterization of antimicrobial compound from *Chromolaena odorata*. J. Phyto. 3, 26–32.
- Suksamrarn, A., Chotipong, A., Suavansri, T., 2004. Antimycobacterial activity and cytotoxicity of flavonoids from the flowers of *Chromolaena odorata*. Arch. Pharmacol. Res. 27, 507–511.
- Taiwo, O.B., Olajide, O.A., Soyannwo, O.O., Makinde, J.M., 2000. Anti-inflammatory, anti-pyretic and antispasmodic properties of *Chromolaena odorata*. Pharm. Biol. 38, 367–370.
- Tian, G., Kolowale, G.O., Salako, F.K., Kang, B.T., 1998. An improved cover crop fallow system for sustainable management of low activity clay soils of the tropics. Soil Sci. 164, 671–682.
- Tian, G., Kang, B.T., Kolowale, G.O., Idinoba, P., Salako, F.K., 2005. Long-term effects of fallow systems and lengths on crop production and soil fertility maintenance in West Africa. Nutr. Cycl. Agroecosyst. 71, 139–150.
- Timbilla, J.A., Zachariades, C., Braimah, H., 2003. Biological control and management of the alien invasive shrub *Chromolaena odorata* in Africa. In: Neuenschwander, P., Borgemeister, C., Langewald, J. (Eds.), Biological Control in IPM Systems in Africa. CABI Publishing, Wallingford, U.K.
- Timmermann, B.N., Mues, R., Mabry, T.J., Powell, A.M., 1979. 6-Methoxyflavonoids from *Brickellia laciniata* (Compositae). Phytochemistry 18, 1855–1858.
- Uyi, O.O., Igbinsola, I.B., 2013. The status of *Chromolaena odorata* and its biocontrol in West Africa. In: Zachariades, C., Strathie, L.W., Day, M.D., Muniappan, R. (Eds.), Proceedings of the Eighth International Workshop on Biological Control and Management of *Chromolaena odorata* and other Eupatorieae, 1–2 November 2010. Nairobi, Kenya. ARC-PPRI, Pretoria, pp. 86–98.
- Uyi, O.O., Ekhaton, F., Ikuenobe, C.E., Borokini, T.I., Aigbokhan, E.I., Egbon, I.N., Adebayo, A.R., Igbinsola, I.B., Okeke, C.O., Igbinsola, E.O., Omokhua, A.G., 2014. *Chromolaena odorata* invasion in Nigeria: a case for coordinated biological control. Manag. Biol. Invasions 5, 377–393.
- Vaisakh, M.N., Pandey, A., 2012. The invasive weed with healing properties: a review on *Chromolaena odorata*. Int. J. Pharm. Sci. Res. 3, 80–83.

- Vijayaraghavan, K., Ali, M.S., Maruthi, R., 2013. Studies on phytochemical screening and antioxidant activity of *Chromolaena odorata* and *Annona squamosa*. *Int. J. Innov. Res. Sci. Eng. Technol.* 2, 7315–7321.
- Wafo, P., Kamdem, R.S., Ali, Z., Anjum, S., Begum, A., Oluyemisi, O.O., Khan, S.N., Ngadjui, B.T., Yakubu, M.T., 2012. Effect of a 60-day oral gavage of a crude alkaloid extract from *Chromolaena odorata* leaves on hormonal and spermatogenic indices of male rats. *J. Androl.* 33, 1199–1207.
- Witkowski, E.T.F., Wilson, M., 2001. Changes in density, biomass, seed production and soil seed banks of the non-native invasive plant, *Chromolaena odorata*, along a 15 year chronosequence. *Plant Ecol.* 152, 13–27.
- Wollenweber, E., Mayer, K., Roitman, J.N., 1991. Exudate flavonoids of *Inula viscosa*. *Phytochemistry* 30, 2445–2446.
- Wollenweber, E., Dorr, M., Muniappan, R., 1995. Exudate flavonoids in a tropical weed, *Chromolaena odorata* (L.) R.M. King and H. Robinson. *Biochem. Syst. Ecol.* 23, 873–874.
- Wollenweber, E., Roitman, J.N., 1996. Novel methyl ether of quercetagenin from *Chromolaena odorata* leaf exudate. *Biochem. Syst. Ecol.* 24, 479–480.
- Younes, A., Hamouda, A., Amyes, S.G., 2011. First report of a novel extended-spectrum beta-lactamase KOXY-2 producing *Klebsiella oxytoca* that hydrolyses cefotaxime and ceftazidime. *J. Chemother.* 23, 127–130.
- Yu, X., He, T., Zhao, J., Li, Q., 2014. Invasion genetics of *Chromolaena odorata* (Asteraceae): extremely low diversity across Asia. *Biol. Invasions* 16, 2351–2366.
- Zachariades, C., Day, M., Muniappan, R., Reddy, G.V.B., 2009. *Chromolaena odorata* (L.) King and Robinson (Asteraceae). In: Muniappan, R. (Ed.), *Biological Control of Tropical Weeds using Arthropods*. Cambridge University Press, Cambridge, pp. 130–162.
- Zachariades, C., Strathie, L.W., Retief, E., Dube, N., 2011. Progress towards the biological control of *Chromolaena odorata* (L.) R.M. King and H. Rob. (Asteraceae) in South Africa. In: Moran, V.C., Hoffmann, J.H., Hill, M.P. (Eds.), *Biological Control of Invasive Alien Plants in South Africa (1999–2010)* vol. 19. *African Entomology*, pp. 282–302.
- Zachariades, C., Janse Van Rensburg, S., Witt, A., 2013. Recent spread and new records of *Chromolaena odorata* in Africa. In: Zachariades, C., Strathie, L.W., Day, M.D., Muniappan, R. (Eds.), *Proceedings of the Eighth International Workshop on Biological Control and Management of *Chromolaena odorata* and other Eupatorieae*, 1–2 November 2010. Nairobi, Kenya. ARC-PPRI, Pretoria, pp. 20–27.
- Zige, D.V., Ohimain, E.I., Nodu, M.B., 2013. Anti-bacterial activity of ethanol, crude and water extract of *Chromolaena odorata* leaves on *S. typhi* and *E. coli*. *Greener J. Microbiol. Antimicrob.* 1, 16–19.