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Review

A review on *Gongronema latifolium (*Utasi): A novel antibiotic against Staphylococcus *aureus* related infections

Etta Hannah Edim[1]*, Uzong Grace Egomi[1], Ekpo Uwem F[2] and Okon Essien Archibong[1]

[1]Biological Science Department, Cross River University of Technology, Calabar, Cross River State, Nigeria.
[2]Department of Biological Sciences, University of Agriculture, Abeokuta, Ogun State, Nigeria.

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Over the years, several reports have appeared on *Gongronema latifolium* a leafy vegetable locally known in the South-eastern part of Nigeria as Utasi or Utazi. The phytochemical constituents, bioactive principles, proximate analyses and chemical compositions of the herb have been reported as well as antimicrobial activities and hypoglycaemic effects. This review present available evidence on the antibiotic efficacy of extracts of *G. latifolium* against, *Staphylococcus aureus* from literature spanning 6 years from 2006 to 2012. We summarized that G. *latifolium* is efficacious for the remedy of abscesses, boils, or furuncle on the skin, treatment of bacteremia and other entero- infections caused by *S. aureus*.

Key words: Utasi, *Gongronema latifolium, Staphylococcus aureus*, antibacterial, biotechnological tool.

INTRODUCTION

Gongronema latifolium (Benth) (Figure 1) (Asclepiadaceae), is a climber with woodyhollow glaborous stems below, and characterized by greenish yellow flowers (Okolo, 1987). It is widespread in tropical Africa and can be found from Senegal east to Chad and south to DR Congo. It occurs in rainforest, deciduous and secondary forests, and also in mangrove and disturbed roadside forest, from sea-level up to 900 m altitude (Chattopadhyay, 1999). The leafy vegetable can be propagated by seed or softwood, semi-hardwood and hardwood cuttings. Fresh seeds have a germination rate of up to 85% at 25 to 29°C. Cold storage for a brief' period improves seed germination. The common name for *G. latifolium* is amaranth globe. In Nigeria *G. latifolium* flowers in July and August. The Efik/Ibibio people in South-eastern Nigeria call the leaves 'Utasi', the Igbos call it 'utazi' and the Yoruba people 'arokeke' or 'madumaro'(Ugochukwu and Babady, 2002). In Ghana, the akan-asantes know it as 'kurutu nsurogya'. The serers in Senegal call it 'gasub', while the kissis, Mende and temnes in Sierra leone call it 'ndondo-polole', 'tawa-bembe' and 'ra-bilong' respectively (Dalziel et al., 1961). They are sharp-bitter and sweet and widely used as a leafy vegetable and as a spice for sauces, soups and salads (Okolo, 1987; Anaso and Onochie, 1999). The leaves are used to spice locally brewed beer. In Sierra Leone the pliable stems are used as chew sticks. The bark contains much latex and has been tested for exploitation (Morebise et al., 2002). The plant has also been widely used in folk medicine for maintaining healthy blood glucose levels (Okafor, 1987, 1989). The plant leaves have been found very efficacious as an anti-diarrhoea and anti-tussive (Sofowora, 1982; Iwu, 1993).

Staphylococcus is a group of bacteria that can cause a number of diseases as a result of infection of various tissues of the body. Staphylococcus -related illness can range from mild and requiring no treatment to severe and potentially fatal. Staph bacteria look like a bunch of grapes or little round berries. They are gram-positive, facultative anaerobic, usually unencapsulated cocci (Todar, 2008). Over 30 different types of Staphylococci can infect humans, but most infections are caused by *S. aureus*. Staphylococci can be found normally in the nose and on the skin (and less commonly in other locations) of around 25 to 30% of healthy adults and in 25% of hospital workers (Enright et al., 2002). In the majority of cases, the bacteria do not cause disease. However, damage to the skin or other injury may allow the bacteria to overcome the natural protective mechanisms of the body, leading to infection. *S. aureus* constitutes a major

*Corresponding author. E-mail: sarahrhoda@yahoo.co.uk.

Figure 1. (*G. latifolium*) Benth.

public health threat, being one of the most common causes of hospital and community acquired infections (Aires-de-Sousa et al., 2006). These organisms are carried by people on skin, in boils, pimples, and throat infections; spread when carriers handle food. *S. aureus* bacteria produce toxins (poisons) at warm temperatures. Meat, poultry, salads, cheese, eggs, custards, and cream-filled desserts are susceptible foods. Food poisoning symptoms include vomiting, diarrhoea, nausea, and abdominal cramps lasting 1 to 2 days (MedcineNet.com, 2011). Staph infections are contagious until the infection has resolved. Direct contact with an infected sore or wound, or with personal-care items such as razors, bandages, etc., are common routes of transmission.

It is on record that half of all *S. aureus* infections in the US are resistant to penicillin, methicillin, tetracycline and erythromycin and vancomycin (Bozdogan et al., 2003). The same can be said of the organism in most parts of the world. According to Prasad et al. (2008), the emergence of multi-drug resistant bacterial strains throughout the globe limits the effectiveness of current drugs and significantly limits treatment, leading to prolonged infections. The increasing resistance of bacteria to antibiotics is kindled due to the misuse and over prescription of the drugs. As resistance to antibiotics spreads, the development of new antimicrobial agents has to be expedited if the problem is to be contained. There is therefore a need to develop new antibiotics to delay or prevent the arrival of a post-antibiotic era (Leggadrio, 1995). Thus the search for newer sources of antibiotics is a global challenge preoccupying research institutions, pharmaceutical companies and academia (Latha et al., 2006).

Until 2006, reports on the antimicrobial effects of *G. latifolium* on *S, aureus* was very scanty. Eleyinmi et al. (2006), however, reported the antimicrobial activity of *G. latifolium* extract against *S. aureus* in their research on the hopping potentials of *V. amygdalina, G. latifolium* and *Garcinia kola* in sorghum larger beer brewing. Extracts from the plant materials were tested against some food spoilage organisms including *S. aureus* using standard procedures, and their results had *G. latifolium* extracts showing greater activity against *B. cereus, B. subtilis, E. coli, E. aerogenes, S. cholerasius ser typhimurium and S. aureus.* In 2007, Essien et al. (2007) reported on the antitussive properties of *G. latifolium* against *S. aureus* tracheal infection in 7-week old broilers. The pet ether leaf extract significantly reduced the mortality rate of the broilers by 25% within 3 weeks (at 10 weeks old) of treatment and by 40% in 6 weeks, when the broilers were 13 weeks of age. These coincided with the reduction in the number of bacteria in the respiratory system of the broilers. The number of aerobic bacteria (including *S. aureus*) in the trachea was reduced from 36 x 10^2 cfu/ml of viscera suspension to 8 x 102 cfu/ml within 3 weeks of treatment. According to them, the ability of Utasi leaves extract to check the proliferation of pathogenic bacteria in the trachea of the sick birds justified its use by local farmers in controlling fowl cough. This also confirmed its antitussive and antidiarrhoeal efficacy in humans confirming age-long use by locales for treatment of diarrhea and cough. According to Eleyinmi (2007) the methanol extracts of *G. Latifolium* showed inhibitory activity against *S. aureus* and several other pathogens, in his study on the chemical composition and antibacterial activity of *G. latifolioum*. The paper disc agar diffusion method was used to screen the pathogens against the antibiotic, ampicillin. He also reported that the aqueous extract had no inhibitory effect on *S. aureus*. Ogbulie et al. (2007) also reported the inhibitory effect of ethanol extract of *G. latifolium* on *S. aureus* from their investigation on the bacterial properties of *G. latifolium* and four other vegetables. Nwinyi et al. (2008), presented results of their investigations on the antibacterial effects of Guava and Utasi against *E. coli* and *S.aureus*. Results obtained show that leaf extracts of both plants possess significant antibacterial activities against the two isolates. Ethanoli extracts showed more inhibitory effect compared to the aqueous extracts. For the extracts of *G. latifolium,* the diameter of zones of inhibition recorded were between 6 and 10 mm while MICs were 10.0 and 2.5 mg ml^{-1} respectively for the aqueous and ethanolic extracts.

Eja et al. (2010) evaluated the anti-microbial synergy of garlic and utasi on *E. coli* and *S. aureus* using the Kirby-Bauer disc diffusion method. Individually, the raw extracts showed appreciable antimicrobial effect (zones of inhibition > 16 mm) on the bacterial isolates with Utasi scoring a ZI of 16 mm and minimum inhibitory concentration (MIC) of 21.3 mg/ml which were high enough to inhibit growth of *S. aureus* colonies. Osuagu and Edeoga (2010) in a study, investigated the effects of fertilizer application on the antimicrobial properties of *G.*

Table 1. Zones of Inhibition (ZI).

Author(s)/year	Type of extract	ZI (mm)	Plant source
Eleyinmi et al. (2006, 2007)	Methanol	7	Akure, Ondo State
	Hot Aqueous	12	
Ogbulie et al. (2007)	Cold Aqueous	8	Dimagu Ideato South, Abia State
	Hot Ethanol	18	
	Cold Ethanol	15	
Nwinyi et al. (2008)	Aqueous	6	Awka, Anambra State
	Ethanol	10	
	Essential oil	8.4	Kosofe, Lagos State
Adeleye et al. (2010)	Aqueous	8.6	
	Ethanol	9	
Eja et al. (2010)	Ethanol	16	Calabar, Cross River State
Osuagu and Edeoga (2010)	Ethanol	13	Umuahia, Abia State
Etta et al. (2012) (unpublished data)	Methanol	13	Calabar, Cross River State

Table 2. Minimum inhibitory concentration (MIC) and minimum bacterial concentration (MBC).

Author(s)	MIC(mg/mL)	MBC(mg/mL)
Eleyinmi et al. (2006, 2007)	Methanol – 5.0	-
Nwinyi et al. (2008)	Aqueous – 10	Aqueous – 10
	Ethanol - 5	Ethanol – 2.5
	Essential oil - 10	Essential oil – 10
Adeleye et al. (2010)	Aqueous - 6.5	Aqueous – 12.5
	Ethanol - 12.5	Ethanol - 12.5
Eja et al. (2010)	Ethanol - 21.3	-
Etta et al. (2012)(unpublished data)	Methanol – ≥ 0.29 ≤ 0.71 (MIC correlates)	-

latifolium and reported that nitrogen, phosphorous, and potassium (NPK) offered a dose-dependent, significant ($P<0.05$) increase of the antimicrobial properties of the ethanol extract of *G. latifolium* against *S. aureus* and some other pathogens. In their study, the control extract showed a ZI of 15 mm while the fertilizer-treated extracts showed ZI s of 23, 26, 25 28 and 30 mm at treatment levels of 100, 200,300,400 and 500 kg/ha respectively. At the observed increased levels of ZI, *G. latifolium* effectively inhibited the microbial activity of the pathogen.

Using the agar-diffusion method, Adeleye et al. (2011), evaluated the essential oil as well as aqueous and ethanolic extracts of *G. latifolium* leaves for antimicrobial activity against bacteria isolated from blood streams of human immunodeficiency virus (HIV) patients. *S. aureus* was one of the isolates.

The essential oils presented an MIC of 5 to 40 mg/ml. For the ethanol extract, the MIC ranged between 3.125 to 12.5 mg mL^{-1} and between 6.25 to 25.0 mg mL^{-1} for the aqueous extract. Minimum bactericidal concentration (MBC) values for the three extracts were also recorded as 5 to 40 µg mL^{-1}, 3.125-25.0 mg mL^{-1} and 6.25-25.0 mg mL^{-1} for essential oils, ethanol extract and aqueous extracts respectively.

In a similar study, Etta et al. (2012) (unpublished data), investigated the antimicrobial properties of Utasi on four pathogenic isolates against a synthetic antibiotic positive control, ciprofloxacin (250 mg). The bacterial cultures were infected with various concentrations of the methanol extract of Utasi and ciprofloxacin as control. The plates were then incubated at 37°C for 24 h. After which the percentage susceptibility and percentage resistance of the isolates and ZI of the extract and the antibiotic were measured. Percentage (%) susceptibility of *S.aureus* to *G. latifolium* extract was 71.4 while percentage resistance was 28.6. The mean ZI was 13 mm. The antimicrobial activity of Utasi against *S. aureus* by different authors are presented in Tables 1 and 2.

DISCUSSION

From all literature gathered, the ZIs and MIC/MBC of recorded are at levels that can inhibit the growth of the gram-positive bacteria *S. aureus* (Figure 2). This would therefore indicate the activity of the plant extract against

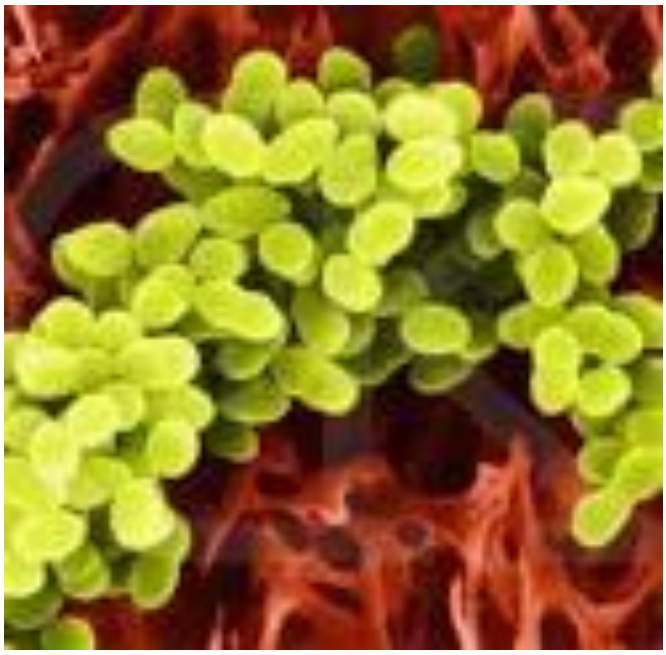

Figure 2. Gram-positive *S. aureus.*

S. aureus related infections. Several reports on the phyto chemical composition of indicate the presence of constituents such as alkaloids, tannins, flavonoids and especially saponnins which have been implicated in the antimicrobial activity of utasi (Ali et al., 1996; Morebise and Fafunso, 1998; Hernández et al., 2000; Oshodi et al., 2004; Eleyinmi et al., 2006, 2007). The antimicrobial properties of flavonoids, saponins and alkaloids have been established (Trease and Evans, 1989). Saponnins have been shown to have a high inhibitory effect on *S. aureus* in previous studies ((Morebise and Fafunso, 1998; Morebise et al., 2002; Soetan et al., 2006; Arora and Kaur, 2009). The presence of essential oils and fatty acids in Utasi have also been established for its' antibacterial properties (Nwinyi, 2008; Eleyinmi, 2007; Adeleye, 2010). The variation in diameter of inhibition (Table 1), maybe due to the method of extract preparation. Powdered seeds showed less antibacterial activity than crushed seeds (Ogbulie et al., 2007; Eja et al., 2010). This could be attributed to inactivation of the active antibacterial substances by the heat generated during grinding of the seeds (using an electric blender) (Arora and Kaur, 2009). The extracting solvent appears to also have a bearing on the antimicrobial activity of the extract on the bacteria. Ethanol extracts seem to give higher ZI than any other extracts. This could be because the active phytochemicals and essential oils in the herb are more soluble in ethanol than in any other solvent (Nwinyi et al., 2008). This corroborates the reports of Obi and Onuoha (2000); Ogueke et al. (2006) and Ogbulie et al. (2007) that ethanol is the best solvent for the extraction of most plant active principles of medicinal importance. The minimum inhibitory concentrations (MIC) which is the minimum concentration that completely inhibits macroscopic microbial growth and the minimal bacteriocidal concentration (MBC), the lowest concentration of the antibiotic that kills 99.9% of the original inoculum in a given time, obtained from reviewed literature also established Utasi as an effective alternative antibiotic (Eleyinmi et al., 2007, 2008; Nwinyi et al., 2008; Adeleye et al., 2010; Eja et al., 2010). Utasi presents as a safe antibiotic that will give the same results as synthetic and non-herbal antibiotics but without the attendant side-effects, for combating staph-related infections even if it acts at a slower pace. Essien et al. (2007) established the antimicrobial effect of Utasi extract on the proliferation of pathogenic bacteria species in the trachea of sick birds. This has also confirmed its antitussive and antidiarrhoeal efficacy in humans. In a recent study, Etta et al. 2012 (unpublished data) recorded MIC correlates of susceptibility and resistance of *S. aureus* to *G. latifolium* methanol extract. The values were ≤0.29 to ≥0.74. These values are high enough to confirm the inhibitory activity of *G. latifolium* against *S. aureus.* This review of literature has brought to fore the unquestionable evidence that Utasi is an emerging novel antibiotic against the gram-positive bacteria *S aureus* hence any staph - related infections. It therefore becomes imperative that the acceptance of Utasi as an antibiotic should move away from our laboratory benches to our pharmaceutical companies. In our search for biotechnological tools for national peace and development, this review would not have come at a better time. Utasi should be given the priority it deserves as a novel plant-based antibiotic and be further characterized to isolate the active ingredient for drug formulation and subsequent clinical trials. New strategies in the pharmaceutical industry to find antimicrobial drugs involve identifying potential molecular targets in cells (such as the active sites of enzymes involved in cell division), then developing inhibitors of the specific target molecule (Todar, 2008). It is our thinking that a phytochemical component in Utasi will produce just the inhibitor required to attack molecular targets in *S. aureus*. We propose initial formulation as an ointment and/or soap for use on infected open wounds, skin infections, boils and pimples for immediate eradication of *S. aureus* colonies. In the nearest future, after in-depth investigations on the mode of action of the active ingredient by clinicians and pharmacists, capsulated, gel-like or even syrupy products can then be formulated. This approach, we believe, could help us win the next round of the fight against yet other antibiotic-resistant bacteria, *S. aureus*.

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