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Species specificity of carbon dioxide, 1-octen-3-ol, l-lactic acid and 2-butanone as mosquito chemo-attractants in mosquito surveillance: A review

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Abstract
Mosquito surveillance is essential for estimation of disease transmission intensity and the evaluation of control measures. Mosquito traps incorporated with synthetic odourants can be used to address surveillance challenges associated with human landing catches, light traps, bed nets occupied by humans, pyrethrum spray catches, and animal baits. The widely used mosquito chemoattractant is carbon dioxide though its application present major challenges, Several researchers have investigated the use of other compounds as carbon dioxide substitutes, these include: 2-butanone, 1-octen-3-ol, acetone, lactic acid, mixed phenols, ammonia and carboxylic acids. Combinations of these chemoattractants have proved to be effective but consequently species specific. The ability of these chemoattractants to target specific species could be used to efficiently estimate the prevalence of particular mosquito-borne diseases, and in mosquito ecological studies so as to focus control and potentially limit occurrence of these diseases.

Keywords: Mosquito, chemoattractants, lactic acid, 1-octen-3-ol, 2-butanone, odourants

1. Introduction

Globally vector borne diseases infect 96 million people and kill over 700,000 people annually [1]. Most of these deaths are from malaria [1, 2]. The disease landscape is continually changing; human impacts such as climate change, travel and commerce have allowed both mosquitoes and diseases to expand their ranges [3]. Africa as a continent experiences the bulk of the global malaria burden due in part to the presence of the *Anopheles gambiae* complex [3]. *Anopheles gambiae* is one of four dominant vector species within the *An. gambiae* complex, the others being *Anopheles arabiensis* and the coastal *Anopheles merus* and *Anopheles melas* [3]. The major mosquitoes of public health importance are summarized in the table below (Table 1), with emphasis on the Afro tropical species. Recent vector control campaigns have resulted in promising declines in incidence and prevalence of these diseases, notably malaria, dengue fever, yellow fever and several encephalitis, but resistance to insecticides and drugs are on the rise [4], threatening to overturn these gains. Moreover several vector-borne diseases have re-emerged, requiring prompt and effective response measures [5]. To improve and properly implement vector control interventions, the behaviour of the vectors must be well understood with detailed examination of mosquito clues in locating human hosts being an essential component [5]. The current vector control strategies have focused mainly on the use of insecticidal nets and indoor residual spraying [6]. Although these methods have seen tremendous reductions in malaria burden especially in sub-Saharan Africa, they are however insufficient to eliminate the transmission of mosquito borne diseases due to growing resistance, operational challenges and dynamic behavioral response of mosquitoes to avoid these interventions [6]. However, a number of substantive opportunities now exist for rapidly developing and implementing more diverse, effective and sustainable malaria vector control strategies for developing countries [6]. Contrary to high-income countries, mosquito control has be substantially achieved through integrated methods comprising environmental management, insecticidal application to outdoor spaces and larval habitats, and mosquito-proof housing [24], most of which remain underused in Africa, hence the need for affordable and easy to use technology like the use of chemoattractants in mosquito baiting [6].

Table 1: Distribution and ecological aspects of mosquito species of public health importance in Africa

Species	Distribution	Remarks	Citations
An. arabiensis An. gambiae	They are found entirely across Africa but mostly occurs in sub Saharan Africa. In Madagascar both species are predominantly zoophilic.	*An. gambiae* is common in the wet season and in high rainfall areas. They are the major vectors of malaria.	[7, 3, 8]
An. melas	It is confined to the west coast of Africa	High organic pollution is typical of the larval habitats.	[7, 3, 8]
An. funestus	It has a wide distribution across Africa but most abundant in the East and West African regions.	Larval habitats typically contain emergent vegetation. Larvae difficult to find: they dive and remain under water for prolonged periods	[7, 9, 8]
Anopheles moucheti	Cameroon, Democratic Republic of Congo, Equatorial Guinea, Gabon, Kenya, Nigeria, Uganda	*An. moucheti* is essentially a forest species and an important vector of malaria in almost all areas where it occurs	[7, 3, 8]
Culex quinquefasciatus	It has a wide distribution almost entirely across Africa and Asia but most occurs in West Africa and some parts of sub Saharan Africa.	*Cx. quinquefasciatus* is common in rapidly expanding urban areas where drainage and sanitation are inadequate	[8, 10]
Ae. aegypti *Ae. albopictus*	Dominant species in sub Saharan Africa. *Ae. albopictus* originally occurred only in Asia and Madagascar but recently invaded North and South America, as well as West Africa.	They are associated with the major outbreaks of dengue fever, yellow fever and several encephalitis	[8, 10]

2. Mosquito surveillance and sampling

Mosquito surveillance is an essential component of a comprehensive mosquito-borne disease prevention and control program [11]. The objective of mosquito surveillance is to determine species composition, geographic distribution, seasonal occurrences, and abundance of potential vectors of mosquito-borne pathogens within each county by collecting and identifying larval and adult mosquitoes [11]. Components of an effective program include: identifying and mapping larval mosquito habitats using ground-based and aerial surveillance methods, identifying and mapping the location of potential vector species within each county through the collection of adult or larval mosquitoes, and testing of potential vector species for mosquito-borne viruses [11]. A sound surveillance program requires a thorough understanding of the biology, ecology and interactions of the vertebrate and mosquito hosts because they determine the transmission rate of arboviruses depends on these interactions [12]. The most widely used methods for sampling mosquitoes have been those using human landing catches, light traps, bed nets occupied by humans, pyrethrum spray catches, and animal baits [12]. Among these, man-landing catches have been the commonly used method for sampling of mosquito vectors and estimation of disease transmission intensity [12]. The methods vary in terms of reliability and efficacy which is creating more need for standardized tools that are sensitive, specific, reliable and ethically acceptable for trapping and sampling mosquitoes [13]. Promisingly, there is an increasing use of mosquito traps for making mosquito collections because these have the advantage of being less labor intensive and the human collectors are not exposed to infective bites [13]. But for these traps to be effective, they must be incorporated with an odourants to attract effectively the mosquitoes. These strategies are based on the idea that disease transmitting mosquitoes locate humans and other blood hosts by identifying their characteristic odour profiles [13].

3. Mosquito chemoattractants

Using their olfactory organs, the mosquitoes detect compounds present in human breath, sweat and skins, and use these as cues to locate and obtain blood from the humans. These odour compounds can be synthesized in vitro, then formulated to mimic humans. In this case, they are called synthetic mosquito lures [13]. Several researchers have investigated these chemical compounds as potential olfactory attractants [14, 13, 15]. These include carbon dioxide (CO_2), acetone, lactic acid, 2-butanone, 1-octen-3-ol (octenol), and mixed phenols [16]. Several studies have demonstrated the role of human odour in the attraction of malaria vectors, as rev, however, few studies attempted to unravel the role of individual chemicals constituting attractive odours [17]. Odourants can be used to control mosquitoes in three complimentary ways: repellents that "push" mosquitoes away, "maskers" that block attraction to humans, and attractants that "pull" mosquitoes into traps placed away from humans [18]. Each of these methods can potentially reduce disease transmission by preventing mosquito-human interactions. Limited field studies evaluating odour-based control find that repellents have been generally better at reducing biting pressure as compared to traps [19, 20, 18]. This is because the current mosquito traps are extremely expensive and bulky, since they need a CO_2 (lure) source, and also may contain other synergists that smell unpleasant [18]. There is therefore an urgent need for new classes of improved mosquito lures for vector control globally.

3.1 Carbon dioxide

Carbon dioxide (CO_2) is one of the important components of human host odour affecting mosquito host-seeking behaviour [21]. It is thought that this gas activates mosquitoes by eliciting take-off behaviour. The presence of CO_2 then sustains the mosquitoes in host-seeking flight [21], guiding them towards their blood meal hosts [17, 15]. The role of carbon dioxide in host-seeking by mosquitoes comprises two distinct actions [22]: Firstly, it acts as an attractant orientation towards the host being mediated by *kinesis* and *optomotor anemotaxis* [22], secondly, it has a combined action with warm moist convection currents at close range and with odour factors at a distance from the host [22], but in terms of attractant effect, carbon dioxide is less powerful than the combined effect of all host factors, both at close range and at moderate distances from the host [22]. The application of this gas from pressurized cylinders, fermenting sugar (say, sucrose or molasses) and the use of dry ice present major challenges to the use of CO_2 based mosquito attractants under field conditions [23]. The gas cylinders are heavy, bulky, expensive and prone to leakages and dry ice can be difficult to obtain, transport and store [25, 9, 26, 24]. Whilst CO_2 produced by fermenting refined sugar or molasses can offer a solution to these problems [27], this method of CO_2 production is also expensive and presents logistical challenges when used on a large scale because the gas is only produced over one trapping night and must be replenished daily [27]. Despite all this, carbon dioxide (CO_2) is the most recognized as a universal mosquito attractant for almost all African anophelines [28, 8].

3.2 1-Octen-3-ol

The role of octenol was first demonstrated on a Glossinidae tsetse fly, *Glossina morsitans* Westwood in the early 1980s [29]. It was later reported to be a mosquito attractant by Takken and Kline in 1989 [14] and since then, a series of field studies have been conducted in a wide variety of ecological habitats to test its efficacy on mosquitoes utilizing the basic experimental design described by Takken and Kline, (I989) [14]. Field studies for example were conducted in estuarine ecosystems in Florida and Georgia [30]. It was discovered that combinations CO_2 and octenol had a synergistic increase in the collections of many mosquito species, especially species of *Aedes* (including *Aedes vigilax* and *Aedes funereus*), *Anopheles*, *Psorophora*, *Coquillettidia*, and *Mansonia* [30]. Another study by Rueda *et al.* (2001), it was discovered that different combinations of attractants had significant increase on the collection of targeted mosquito species especially where combinations of octenol and CO_2 were used with minimal differences in notable species of *Aedes vexans*, *Anopheles crucians* and *Anopheles punctipenni* [31]. These studies therefore clearly show that octenol is not an effective attractant on its own but rather in combination with carbon dioxide [31]. Hence, octenol is most effective in trapping systems on *Aedes* mosquitoes (including *Ae. taeniorhynchus*) and only a few *Culex* mosquitoes [33]. This provides optimism that a control strategy against such mosquitoes can be devised using this semio-chemical [32, 33].

3.3 2-butanone

Turner *et al.* (2011) identified 2-butanone as a potential replacement for CO_2 in a synthetic blend of mosquito attractants [34]. These authors demonstrated the capacity of 2-butanone to induce a dose-dependent activation of the cleavage product A (cpA) carbon dioxide receptor neuron in the maxillary palps of *An. gambiae, Ae. aegypti* and *Cx. quinquefasciatus* [34]. In 2017, Mburu *et al.* went further to investigate the possibility of using 2-butanone as a carbon dioxide mimic in attractant blends for the Afro tropical malaria mosquitoes *An. gambiae* and *An. funestus* [23]. They shown that female *An. gambiae* mosquitoes can be attracted to baits containing 2-butanone alone and 2-butanone+carbon dioxide mixture than other variants [23]. In addition, 2-butanone gave increased catches of wild female *An. funestus* to traps too [23]. These results therefore, demonstrate that 2-butanone is an effective synthetic of host-seeking *An. gambiae* sensu lato and *An. funestus* mosquitoes [23].

3.4 L-(+)-lactic acid

Lactic acid is chiral, consisting of two optical isomers [35]. One is known as L-(+)-lactic acid or (S)-lactic acid and the other, its mirror image, is D-(−)-lactic acid or (R)-lactic acid [35]. However, D-(−)-lactic acid is less attractive than L (+)-lactic acid [35]. Davis and Sokolove, (1976) were among the first to show the influence of lactic acid on mosquitoes but identifying a pair of chemoreceptor neurons sensitive in the grooved-peg sensilla on the antennae of the *Ae. aegypti* mosquitoes [36]. Several other studies have demonstrated the efficiency of L-(+)-lactic acid as a mosquito lure. For example L (+)-lactic acid at the concentrations given off by human hands has been shown to be an attractant for avid female *Ae. aegypti* (L.) [35]. In addition, it was also discovered that L (+)-lactic acid together with ammonia, formed the most attractive blend to *Ae. aegypti* (L.) mosquitoes only when used in combination with two fatty acids each from a different group of carboxylic acids: C1–C3 and C5–C8 [37, 38]. Smallegange *et al.* (2005) investigated the effect of ammonia, lactic acid and carboxylic acids on naive female mosquitoes using a dual-port olfactometer. Contrary to what had been discovered before, ammonia was an attractant on its own, whereas lactic acid was not attractive even when combined with ammonia [39, 38]. However, a synergistic effect was only found when ammonia, lactic acid and the carboxylic acids were applied as a blend to *An. gambiae* Giles sensu stricto [39]. This therefore clearly shows that L-lactic acid is an effective attractant only when combined with ammonia, and carboxylic acids in its orientation to human hosts, especially with *An. gambiae* mosquitoes. Despite all these studies, some researchers [40], have gone further to suggest that L-lactic acid is a mosquito repellent at certain concentrations rather than being a mosquito attractant. Shirai *et al.* (2001) in their studies shown than L-lactic acid exhibited both relative and absolute repellency properties when tested on *Ae. albopictus* (Skuse) mosquitoes [40].

The major concepts regarding the efficacy of various mosquito chemoattractants are summarized in Table 2.

Table 2: Summary of the roles of mosquito chemoattractants on mosquito species

Compound	Mosquito species	Remarks	Citations
Carbon dioxide	Almost all anophelines including: *An. crucians, An. punctipenn, An. quadrimaculatus* and *An. gambiae; Cx. quinquefasciatus, Ae. taeniorhyrrchus, Arwphcles spp., Wymmyia nxitchellii, Ae. vexans, Ae. aegypti*	Female mosquitoes are sensitive to changes in carbon dioxide concentrations as low as 0.01% and when concentrations exceed 4.0%, the mosquitoes senses are considered saturated	[22, 14, 28, 31, 41, 42, 43, 15, 44, 26]
2-butanone	*An. gambiae, Ae. aegypti, Cx. quinquefasciatus*	2-butanone as a lure alone	[34]
	An. arabiensis, An. fenestus, An. gambiae s.l.	2-butanone + carbon dioxide	[23]
1-octen-3-ol	*Ae. albopictus*	Octenol + lactic acid	[45]
	Ae. vigilax Skuse, *Ae. fenerus* Theobald, *An. vexans, An. punctipenni, An. crucians*	Octenol + carbon dioxide	[29, 32, 46, 31]
	Culex spp. including *Cx. impunctatus, Cx. nigripalpus and Cx. erraticus; Ochlerotatus infirmatus; Psorophora spp. including Psorophora ferox; An. gambiae, Aedes spp.*	Octenol as a lure alone	[43, 45, 47]

	including Ae. aegypti, An. spp.; Culiseta spp.; Mansonia spp.; Wyeomyia spp.		
L-lactic acid	*Ae. aegypti, An. gambiae, Cx. pipiens; Ae. atropalpus*	L-lactic acid as the mosquito lure alone	[35, 36, 48, 37, 49, 43]
	Ae. taeniorhynchus	Lactic acid + phenols	[32]
	An. gambiae, *Ae. aegypti* and various *Aedes* mosquitoes	Ammonia + lactic acids + carboxylic acid	[17, 37, 39, 43, 38, 15]

4. Conclusion

The central goal of developing potent mosquito attractants lies in vector control and surveillance [43, 45], a huge impact of which can be achieved through mass trapping [16], lure and kill technology [50, 45] or lure and contaminate technology of target mosquito species. The ability of mosquito lures to attract specific mosquito species can be used as a strategy of eliminating most deadly species especially those transmitting malaria, dengue, yellow fever and Zika virus and potentially limit occurrence of those diseases.

4.1 Declarations

The authors declare that they have no competing interests.

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