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Case Study

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Alcohol, Smoking and Chewing Tobacco-Risk factors for Malaria and Dengue Transmission?–A Case Control Study

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ABSTRACT

Mosquitoes transmit many life-threatening infections to humans. They are attracted to human beings by specific chemical emissions from our body including carbon dioxide, lactic acid and oct-3-enol. Some of these chemicals are present in tobacco and alcohol implying that chronic alcoholics and tobacco smokers may stand at a higher risk for being infected with mosquito borne diseases like malaria and dengue. The study was a hospital based, case control study in the Government general hospital, Guntur, India, over a period of five months. We compared the proportion of alcohol and tobacco abusers in mosquito borne disease patients [n=77] with that of controls [n=82]. The mean pack years of tobacco smoking in cases was lower [3.7±2.8] than in controls was [6.5±2.3] (p= 0.04).The percentage of tobacco users [chewing and/or smoking] was not higher in patients afflicted with mosquito borne diseases [malaria and dengue put together] than in controls. The proportion of alcohol consumers also was not different in cases and controls.

Keywords: Malaria; Dengue; Mosquito borne diseases; Alcohol; Tobacco; Mosquito repellent; Mosquito attractant.

1. INTRODUCTION

Mosquito borne diseases including malaria, dengue, chikungunya (Tolle, 2009) and the recent epidemics of zika (Ioos *et al.,* 2014) pose a major public health challenge all over the world. World-wide the diseases afflict over a million people every year (Tolle, 2009). Although they were initially restricted to the equatorial regions, currently these diseases are also reported in the temperate regions. The expansion of these particular vector borne diseases is attributed to the rising temperatures of the atmosphere across the world due to global warming which provides warm favorable breeding niches for mosquitoes even at higher latitudes (Reeves *et al.,* 1994).

Female mosquitoes transmit diseases when they seek and obtain human blood for egg production (Gulia-Nuss *et al.,* 2011). They identify and approach human beings principally by using their powerful olfactory sense (Lefèvre *et al.,* 2010). They are selectively attracted to specific concentrations and composition of human body odour emanations like carbon dioxide, lactic acid, ammonia (McBride, 2016) and oct 3 enol (Kline, 1994) that vary from person to person. This partly explains why mosquitoes bite certain individuals more than others. It can therefore be expected that any substance that increases human body emissions of mosquito attractants like carbon dioxide, is more likely to enhance mosquito bites and incidence of mosquito borne diseases (Takken and Knols, 1999; Zwiebel and Takken, 2004; Verhulst *et al.,* 2013).

Tobacco and alcohol are two of the most commonly abused agents. Tobacco smoke is known to contain substances like ammonia (Van amsterdam *et al.,* 2011) and enols (Lisko *et al.,* 2014). A study by *Dieng et al.,* in 2011 demonstrated that mosquitoes are attracted to cigarettes (*Dieng et al.,* 2011). However there is a need to find out whether smoking of tobacco can be a risk factor for mosquito borne diseases like malaria and dengue.

Alcoholic beverages also contain mosquito attractants like carbon dioxide. Many wines contain oct-3-enol which is a powerful mosquito attractant (Steel *et al.,* 2014). Alcohol ingestion also increases the lactic acid in blood and body fluids (MacDonald *et al.,* 1994). Experiments have shown that intake of beer makes the individuals attractive to mosquitoes (Lefèvre *et al.,* 2010; Shirai *et al.,* 2002). It is postulated that consumption alcohol may increase the production of the powerful mosquito attractant, l-octen-3-ol (Lefèvre *et al.,* 2010). Therefore this study hypothesized that people abusing tobacco and alcohol may be more attractive to disease transmitting mosquitoes and may be at higher risk of contracting mosquito borne diseases. Thus the following objectives were investigated. (i) The proportion of mosquito borne diseases in patients abusing alcohol. (ii) The proportion of mosquito borne diseases in patients abusing tobacco.

In real world many factors including other surrounding smells, use of repellants, temperature changes, wind and relative humidity affect the interaction between the human body odour and host-seeking mosquitoes. The potential for tobacco and alcohol abuse as risk factors for mosquito borne diseases can be assessed only by real world study.

2. METHODS

We conducted a case control study to compare the use of tobacco and alcohol in cases of malaria and dengue with controls without these diseases. The study was a case control in compliance with STROBE guidelines. We visited 176 male patients who were admitted in a government general hospital at Guntur (malaria and dengue endemic area with high incidence in the monsoon months of July to November), India between August, 2015 and December 2015. Seventy seven out of 159 patients suffered from malaria, dengue or both. The rest of the patients did not have these diseases or a documented history of these diseases in the past. Of the 176 male patients, 17 were excluded from the study due to inadequate history and poor communication. A sample size of 250 cases and controls combined was calculated [assuming that patients with alcohol and tobacco abuse are at least twice as they are likely to be associated with malaria and/or dengue infection as controls] with 80% power and 95% confidence from a pilot study on 20 subjects. The study was restricted to 159 patients due to the end of the monsoon season after which cases were reported very sparsely to our institution (Figure 1). All patients with evidence of malaria based on dry smear or rapid antigen test [antigen detection of *Plasmodium falciparum and P. malariae* by ADVANTAGE MALARIA CARD, J.Mitra & Co, India] and dengue by rapid test [Dengue NS1 antigen and IgM by Dengue Day 1 Test, J. Mitra & Co, India] between the ages 10–80 years were included. All female patients were excluded as the abuse of tobacco and alcohol by women in this geographical region is very miniscule compared to men. Controls were recruited from inpatients of the same medical wards with non mosquito borne diseases to avoid confounding effects due to socio economic and regional factors. Other than that, no specific matching was done. Patients who had quit tobacco smoking and alcohol consumption one month prior to the onset of febrile symptoms were excluded from the study. Patients were sub grouped as those infected with dengue and malaria for further analysis as each of the disease is transmitted by a different mosquito species. Written informed consent was obtained from all participants. The study was approved by the institutional ethical committee of Guntur Medical College, Guntur.

Demographic data of the patients such as age, sex, occupation and residence were recorded.

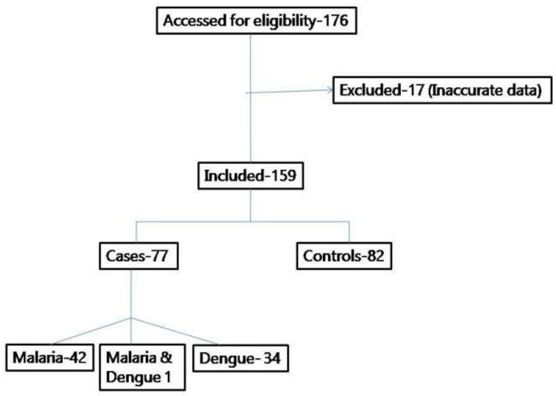

Figure 1: Study outline.

Tobacco

The patients also provided information on the quantity, duration and habit of tobacco smoking, and tobacco chewing. The proportion of patients associated with tobacco abuse in mosquito borne disease patients was compared with that of controls.

Alcohol

The patients also provided information on the quantity, duration and habit of alcohol consumption. The proportion of patients associated with alcohol abuse in mosquito borne disease patients was compared with that of controls.

Statistics

All missing data was excluded from analysis. Quantitative data such as age of the subjects, duration of tobacco use were described by mean and standard deviation and analyzed by student independent t test. Qualitative data including sex, occupation, residence, malaria and dengue infection, alcohol and tobacco abuse were described by percentage and analyzed by chi-square test with a two sided p value < 0.05 taken as statistically significant. Nonparametric quantitative data was log transformed for analysis. The effect of age, occupation and residence on difference in tobacco and alcohol usage between cases and controls was analyzed using multiple logistic regression. The data was recorded and analyzed using IBM SPSS version 20.

3. RESULTS

Amongst the cases, the proportion of urban populace was more than the rural population (Table 1). There were significant differences in the occupations of the two groups (p=0.02). Most of the patients (75.3%) were employed in occupations with manual labor.

Tobacco

The mean pack years of tobacco smoking in cases was 3.7±2.8 and in controls was 6.5±2.3 (p= 0.04). However, the percentage of tobacco users (chewing and/or smoking) was not higher in patients afflicted with mosquito borne diseases (malaria and dengue put together).

Alcohol

The proportion of alcohol consumers also was not different in cases and controls (Figure 2).

Dengue

Amongst patients with dengue, tobacco users were less in proportion when compared to those in controls (Figure 3). Non tobacco users were 2.26 [0.96-5.3] times likely to be associated with dengue infection (p=0.057). After adjusting for the effect of age, occupation, residence and alcoholic status the odds decreased to 1.3 (p=0.7). Non alcoholics were 3.18(1.33-7.62) times likely to be associated with dengue infection (Figure 3) (p=0.008). After adjusting for the effect of age, occupation, residence and tobacco consumption, the odds were 0.2 times higher than in controls (p=0.05).

Malaria

Percentage of tobacco users [chewing and/or smoking] was not different among malaria infected patients (55.8% vs 52.4%, p=0.7). The proportion of alcohol consumers (58.1% vs 54.9%, p=0.7 (were also was not different in cases and controls (Figure 4).

Table 1: Baseline Comparison of patients and controls

	Cases (Malaria and Dengue) (n=77)		Control (n=82)	Malaria (n=43)	Dengue (n=35)
Mean Age (SD)		35 (15)	38 (14)	36 (13)	31 (15)
Occupation%	Student	13	9.3	4.7	25.7
	Job/business	6.5	12	9.3	2.9
	Laborer /Farmer	75.3	74.7	81.4	65.7
	Retired	5.2	4	4.7	5.7
Residence%	Urban	70.1	51.9	69.8	71.5

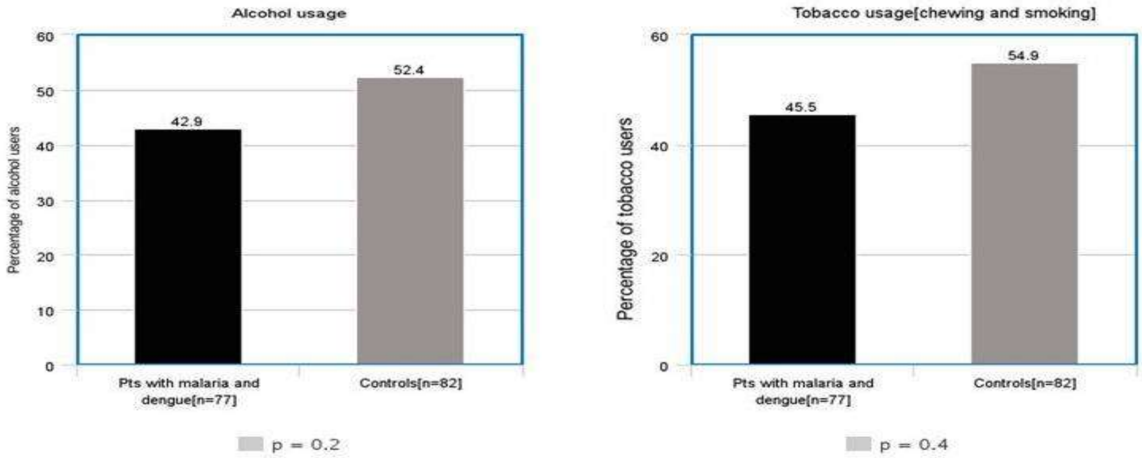

Figure 2: Comparatively similar percentage of tobacco and alcohol abusers in the cases and controls.

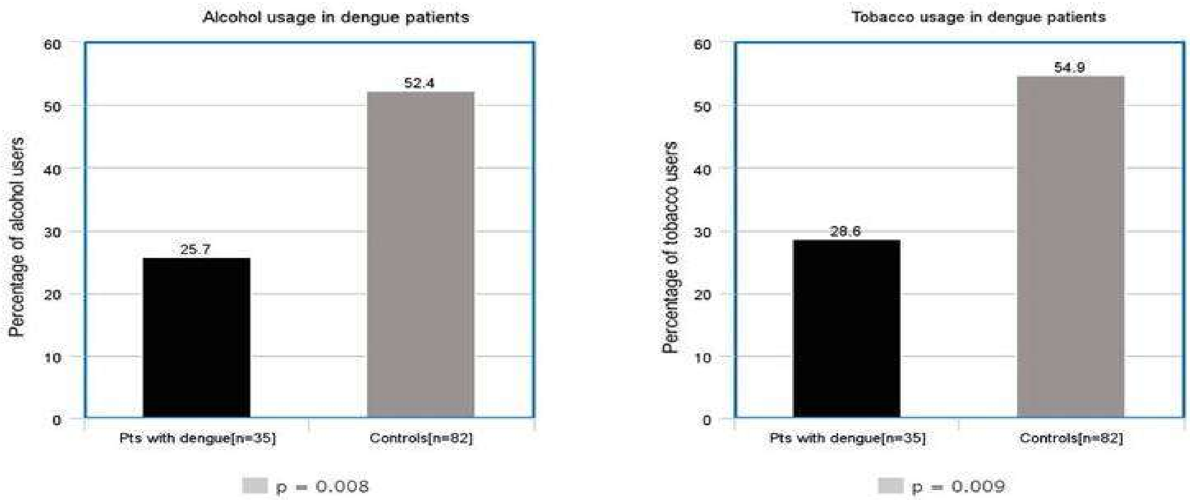

Figure 3: Higher percentage of tobacco and alcohol abusers in the controls than in the dengue patients.

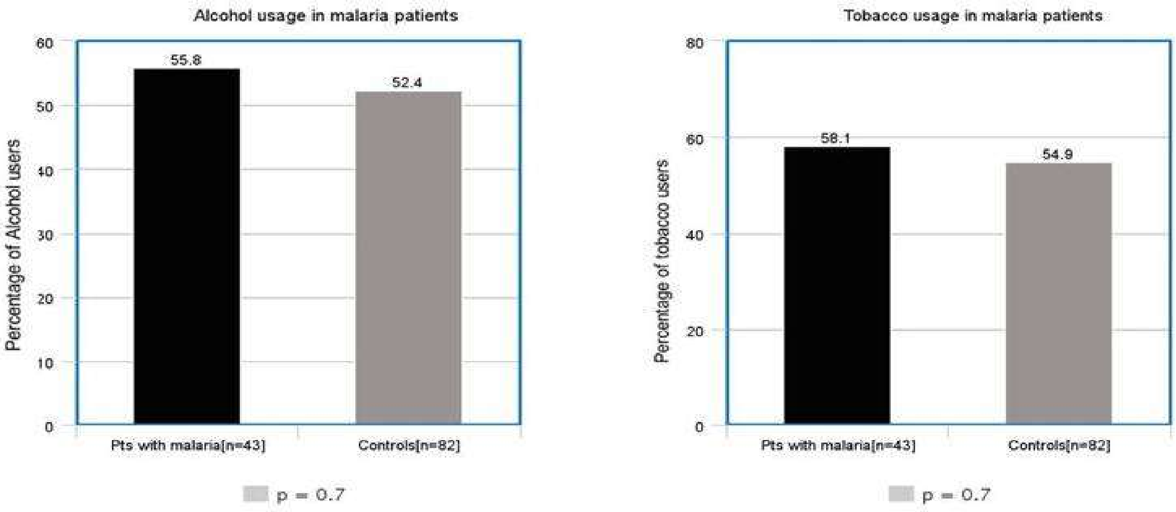

Figure 4: Similar percentage of tobacco and alcohol abusers in the malaria patients and controls.

4. DISCUSSION

This is the first real world scenario study to understand the association between mosquito borne diseases and tobacco and alcohol.

We found that proportion of alcohol consumers and tobacco users were similar between patients with mosquito borne diseases (malaria and dengue) and control population. But heavier smokers (number of pack years) appear to be less associated with mosquito borne diseases.

The absence of difference in proportion of smokers and alcohol abusers between cases and controls may also be due to an important factor. A mosquito in order to be able to transmit the parasite has had to have bitten an infected person initially. In general, sick and bed ridden patients might avoid alcohol or tobacco. Therefore even though the mosquitoes which are known to be attracted to the high concentration of smoking/alcohol induced chemicals such as ammonia, carbon dioxide and lactic acid bite the abusers of alcohol and tobacco much more than other people, they may not capture the parasite for transmission as they may not be in a sick parasite carrying state in the first place while consuming alcohol or tobacco.

Environmental factors also play an important role in the process of olfaction as the smells are carried through the air. A high degree of relative humidity in the atmosphere helps mosquitoes to detect odours easily (Shirai *et al.,* 2002). The city of Guntur is in the heart of South India with the climate being dry and hot most of the year. Thus, this climate may not be conducive to olfaction of the mosquitoes and may have affected the results.

Subgroup analysis showed that, non alcoholics and non smokers were more in proportion in the dengue patient group when compared to controls (Figures 3 and 4). This may be due to the differences in the preferences of the two mosquitoes, *Anopheles* and *Aedes* (McBride, 2016). Dengue virus transmitting mosquito *Aedes aegypti* might be repelled by the odour of tobacco and alcohol. For example, eugenol (Lisko *et al.*, 2014) an important constituent of additives to tobacco is known to repel *Aedes* mosquitoes (Menger *et al.,* 2014). Other flavouring agents used in tobacco products such as linalool, δ-decalactone, and δ-undecalactone (Paschke *et al.,* 2015). are also strong *Aedes* mosquito repellents (Menger *et al.,* 2014).

However more studies on these three compounds are needed as they are dispensed in combination with other chemicals produced by burning tobacco.

Similarly alcohol also contains chemicals that are known mosquito repellents. Eugenol, gerniol (Eyres *et al.,* 2007), linalool (Steinhaus *et al.,* 2003), phenylethanol (Langos *et al.,* 2013) and δ-decalactone (Poisson and Schieberle 2008) are used in the preparation of many alcoholic beverages. These are also components of mosquito repellent preparations (Menger *et al.,* 2014; Bissinger *et al.,* 2015). Many of the carboxylic acids present in alcohol (Reeves *et al.,* 1994) are also repellent to mosquitoes (Smallegange *et al.,* 2005).

Studies have shown that excessive attractants may also act as repellents at high concentrations (Kennedy, 1978). This has been clearly shown with ammonical odour. Ammonia is attractive to mosquitoes up to 13,637 ppm and clearly repulsive at 1,36,371 ppm. Another important contributing factor is that a blend of ammonia and lactic acid combined act as mosquito repellent (Smallegange *et al.,* 2005). Ammonia is a major constituent of cigarettes (Van amsterdam *et al.*, 2011) and lactic acid increases in the blood with intake of ethanol (Kennedy, 1978). Their repellent action might result in the lower proportion of dengue cases in patients using alcohol and tobacco in this study.

As of now the evidence for the use of repellents based on odour similar to alcohol and tobacco against malaria and dengue transmitting mosquitoes is unclear. They may not be useful as attractants either (for mosquito borne disease research).

These results can be limited by the small sample size of our study. Also the effect of other environmental and host odours could not be assessed by the study design and asymptomatic and mildly symptomatic patients may have been missed as this was a hospital based study. This study also does not estimate the number of mosquito bites and so may not accurately reflect the attraction power of alcohol and tobacco odours. Use of a case-control study design is more appropriate when the incidence rate of an outcome is low and the disease has a long latency. The investigators had prior knowledge of the case or control status of the respondents. This could be a source for bias in this study.

To conclude, tobacco and alcohol use does not appear to increase the risk of infection with mosquito borne diseases like malaria and dengue. The influence of alcohol and tobacco odour on Aedes mosquitoes and dengue infection needs to be explored further.

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Conflicting of Interests

Declare to none.

References

1. Bissinger BW, Kennedy MK, Carroll SP. Sustained efficacy of the novel topical repellent TT-4302 against mosquitoes and ticks. *Med Vet Entomol.* 2015; 30(1): 107-111.
2. Dieng H, Saifur RGM, Ahmad AH *et al.,* Discarded Cigarette Butts Attract Females and Kill the Progeny of *Aedes albopictus. J Am Mosq Control Assoc.* 2011; 27(3): 263-271.
3. Eyres GT, Marriott PJ, Dufour JP. Comparison of odor-active compounds in the spicy fraction of hop (*Humulus lupulus* L.) essential oil from four different varieties. *J Agric Food Chem.* 2007; 55(15): 6252–6261.

4. Gulia-Nuss M, Robertson AE, Brown MR, Strand MR. Insulin-Like Peptides and the Target of Rapamycin Pathway Coordinately Regulate Blood Digestion and Egg Maturation in the Mosquito *Aedes aegypti.* PLoS ONE. 2011; 6(5): e20401.
5. Ioos S, Mallet HP, Leparc Goffart I *et al.,* Current Zika virus epidemiology and recent epidemics. *Médecine Mal Infect.* 2014; 44(7): 302-307.
6. Kennedy JS. The concepts of olfactory "arrestment" and "attraction." *Physiol Entomol.* 1978; 3(2):91-98.
7. Kline DL. Olfactory attractants for mosquito surveillance and control: 1-octen-3-ol. *J Am Mosq Control Assoc.* 1994; 10(2 Pt 2): 280-287.
8. Langos D, Granvogl M, Schieberle P. Characterization of the key aroma compounds in two bavarian wheat beers by means of the sensomics approach. *J Agric Food Chem.* 2013; 61(47): 11303-11311.
9. Lefèvre T, Gouagna LC, Dabiré KR *et al.,* Beer consumption increases human attractiveness to malaria mosquitoes. PloS One. 2010; 5(3): e9546.
10. Lisko JG, Stanfill SB, Watson CH. Quantitation of Ten Flavor Compounds in Unburned Tobacco Products. *Anal Methods Adv Methods Appl.* 2014; 6(13): 4698-4704.
11. MacDonald L, Kruse JA, Levy DB, Marulendra S, Sweeny PJ. Lactic acidosis and acute ethanol intoxication. *Am J Emerg Med.* 1994; 12(1): 32-35.
12. McBride CS. Genes and Odors Underlying the Recent Evolution of Mosquito Preference for Humans. *Curr Biol CB.* 2016; 26(1): R41-46.
13. Menger DJ, Van Loon JJA, Takken W. Assessing the efficacy of candidate mosquito repellents against the background of an attractive source that mimics a human host. *Med Vet Entomol.* 2014; 28(4):407-413.
14. Paschke M, Hutzler C, Henkler F, Luch A. Toward the stereochemical identification of prohibited characterizing flavors in tobacco products: the case of strawberry flavor. *Arch Toxicol.* 2015; 89(8):1241-1255.
15. Poisson L and Schieberle P. Characterization of the key aroma compounds in an american bourbon whisky by quantitative measurements, aroma recombination, and omission studies. *J Agric Food Chem.* 2008; 56(14): 5820–5826.
16. Reeves WC, Hardy JL, Reisen WK, Milby MM. Potential effect of global warming on mosquito-borne arboviruses. *J Med Entomol.* 1994; 31(3):323-332.
17. Shirai O, Tsuda T, Kitagawa S *et al.,* Alcohol ingestion stimulates mosquito attraction. *J Am Mosq Control Assoc.* 2002; 18(2): 91-96.
18. Smallegange RC, Qiu YT, Loon JJA van, Takken W. Synergism between ammonia, lactic acid and carboxylic acids as kairomones in the host-seeking behaviour of the malaria mosquito *Anopheles gambiae* sensu stricto (Diptera: Culicidae). *Chem Senses.* 2005; 30(2): 145-152.
19. Steel CC, Blackman JW, Schmidtke LM. Grapevine bunch rots: impacts on wine composition, quality, and potential procedures for the removal of wine faults. *J Agric Food Chem.* 2013; 61(22): 5189-5206.
20. Steinhaus M, Fritsch HT, Schieberle P. Quantitation of (R)- and (S)-linalool in beer using solid phase microextraction (SPME) in combination with a stable isotope dilution assay (SIDA). *J Agric Food Chem.* 2003; 51(24): 7100–7105.
21. Takken W and Knols BG. Odor-mediated behavior of Afrotropical malaria mosquitoes. *Annu Rev Entomol.* 1999; 44: 131–157.
22. Takken W, Knols BGJ, Otten H. Interactions between physical and olfactory cues in the host seeking behaviour of mosquitoes: The

role of relative humidity. *Ann Trop Med Parasitol.* 1997; 91(Supplement 1): 119–120.
23. Tolle MA. Mosquito-borne Diseases. *Curr Probl Pediatr Adolesc Health Care.* 2009; 39(4): 97–140.
24. Van amsterdam J, Sleijffers A, van Spiegel P *et al.*, Effect of ammonia in cigarette tobacco on nicotine absorption in human smokers. *Food Chem Toxicol.* 2011; 49(12): 3025–3030.
25. Verhulst NO, Loonen JA, Takken W. Advances in methods for colour marking of mosquitoes. *Parasit Vectors.* 2013; 6: 200.
26. Zwiebel LJ and Takken W. Olfactory regulation of mosquito–host interactions. *Insect Biochem Mol Biol.* 2004; 34(7): 645–652.

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