Pask G. M. *et al* (2013) Chem. Senses 38: 19 – 25 "The molecular receptive range of a lactone receptor in *Anopheles gambiae*". This scientific article describes the testing of a range of lactone compounds found in nature and which are the basis of many natural odours, e.g. emitted by fruits. AgOr48 is the odorant-sensitive OR lactone receptor from *An. gambiae*. AgOr48 is heterologously expressed in a human cell line and voltage-clamp and calcium imaging are used to investigate the molecular receptive range of the receptor. No particular functional significance is attached to any of the lactones tested. Delta-undecalactone is only one of a number tested. The authors suggest that the lactone specificity of AgOr48 plays a role in the attraction of mosquitos to sugar sources.

There is an urgent need for additional and/or improved insect repellent compounds. The inventors have surprisingly found that δ-decalactone and δ-undecalactone each have significant mosquito repellent activity which is similar to or better than that of DEET. Moreover, whereas the activity of DEET has no spatial effect on distances from the human skin greater than a few millimeters, δ-decalactone and δ-undecalactone both have a significant repellent effect from a distance of at least several decimeters.

DISCLOSURE OF THE INVENTION

Accordingly, the present invention provides an insect repellent composition comprising δ-decalactone and/or δ-undecalactone wherein the δ-decalactone and/or δ-undecalactone is formulated for topical application to a human or animal. Also disclosed is δ-decalactone and/or δ-undecalactone for use as an insect repellent.

In another aspect, there is provided an insect repellent composition for making articles, fabric, textile, mesh or net comprising δ-decalactone and/or δ-undecalactone in the form of a synthetic resin; preferably wherein the δ-decalactone and/or δ-undecalactone is at a concentration of at least 1% (w/w).

In yet another aspect, there is provided an article or a material coated and/or impregnated with δ-decalactone and/or δ-undecalactone; preferably at least 1% (w/w) δ-decalactone and/or δ-undecalactone; and preferably wherein the article or material is selected from a fabric, textile, mesh or net.

In yet another aspect, there is provided an insect repellent apparatus comprising a container containing a composition comprising δ-decalactone and/or δ-undecalactone; preferably

wherein the container is in fluid connection with an orifice which can be exposed to the air, or a porous surface which can be exposed to the air.

In yet another aspect, there is provided use of δ-decalactone and/or δ-undecalactone as an insect repellent.

In yet another aspect, there is provided a push-pull system of insect control comprising insect repellent apparatus as described herein, and a spatially separate insect attractor, optionally included as part of a trap or killer.

In yet another aspect, there is provided a method of controlling insects in an area, comprising releasing δ-decalactone and/or δ-undecalactone into the air at one or more locations in and/or outside of the area.

δ-decalactone and/or δ-undecalactone are volatile liquid compounds at room temperature. The inventors consider that these compounds exert their repellent effect when in the airspace that the insects come into contact with. Therefore, the active compound(s) of the disclosure are preferably provided for use in a suitable vehicular form, such as a solid, semi-solid, gel, liquid, either or not micro-encapsulated, from which the compounds may volatilize or be volatilized, for example, by heating and/or venting. If in the form of a liquid, volatilization may be achieved by spraying, for example.

δ-decalactone may be used separately of and from δ-undecalactone in providing an insect repelling effect. However, a combination of the two compounds may also be used in a suitable ratio.

δ-decalactone or δ-undecalactone, when used as an insect repellent in accordance with any aspect of the invention may be undiluted, i.e. 100% (v/v) liquid form of the compound.

Preferably though, the δ-decalactone or δ-undecalactone will be used in a less concentrated form, for example in a suitable vehicle in a concentration of from about 0.1% to about 99% (v/v). In preferred examples, the δ-decalactone or δ-undecalactone is provided at a concentration in suitable vehicle of about 0.25% to about 75% (v/v); preferably from about 0.5% to about 50% (v/v); even more preferably about 0.75% - 25% (v/v). An effective composition may comprise about 1% (v/v) in a suitable diluting vehicle.

As a vehicle or carrier employed in forming liquid formulations, there may be used, for example, alcohols such as ethanol, glycerin and polyethylene glycol; acetone, ethers such as tetrahydrofuran and dioxane; aliphatic hydrocarbons such as hexane, kerosine, paraffin and petroleum benzene; and esters such as ethyl acetate. The liquid formulation may be impregnated into different types of textile fabrics, such as cotton, polyamides (nylon), polyesters, super-absorbent gels (SAPs) or suitable mixtures of these.

A preferred dilution vehicle is an alcohol, e.g. ethanol. In the case of δ-decalactone the vehicle is preferably an oil, for instance a mineral or vegetable oil.

When used in combination, the aggregate concentration of δ-decalactone or δ-undecalactone may be 100% (v/v) or fall within one of the aforementioned ranges of concentration in a suitable vehicle.

δ-decalactone and δ-undecalactone when used as described above, may further be used in combination (as aforementioned), separately, sequentially or simultaneously. When used separately, δ-decalactone and δ-undecalactone may be used in same or different vehicles at same or differing concentration.

In other examples, the δ-decalactone and/or δ-undecalactone may be used with a further insect repellent. When used in combination simultaneously there is a mixture of the repellents in the composition, optionally in a suitable vehicle.

When a further insect repellent is used separately with the δ-decalactone and/or δ-undecalactone (whether or not simultaneously), the further insect repellent may be present in the same or a different type of vehicle, but not in the form of a mixed composition with the δ-decalactone and/or δ-undecalactone. For example, δ-decalactone may be provided in an oleaginous form, whereas the further insect repellent (other than δ-undecalactone) may be provided separately in an organic solvent.

Whether a further insect repellent is presented in the same or different type of vehicle as that used for δ-decalactone and/or δ-undecalactone, and whether or not as a mixture with the δ-decalactone and/or δ-undecalactone, the further insect repellent may be used together with the δ-decalactone and/or δ-undecalactone in an area or airspace in a spatially and/or temporally separate manner. This may be spatially and/or temporally distinct.

In other examples there may be at least partial spatial and/or temporal overlap of release of δ-decalactone and δ-undecalactone. In examples involving further insect repellents, there may be at least partial spatial and/or temporal overlap in release of the further repellents with the release of δ-decalactone and δ-undecalactone into the air.

Any further insect repellent may be selected from 6-methyl-5-hepten-2-one (6MHO), linalool (LNL), N,N-diethyl-meta-toluamide (DEET) and *p*-Menthane-3,8-diol (PMD), for example. However, any suitable further insect repellent substance may be used, including natural products.

δ-decalactone and/or δ-undecalactone when used in accordance with any examples of the disclosure as defined above may be used in combination with a spatially separate insect attractant or trap, so as to create a push-pull form of insect control.

In alternative example, the invention includes δ-decalactone and/or δ-undecalactone for use as an insect repellent, wherein the δ-decalactone and/or δ-undecalactone is formulated for topical application on a human or animal.

In any example, the insect is of the order Diptera, and preferably a mosquito; preferably wherein the mosquito is of a species or subspecies of a genus selected from *Anopheles*, *Aedes, Culex, Culiseta, Haemogogus, Mansonia* and *Psorophora.* The present disclosure is preferably applied to dealing with a species or subspecies of mosquito of the genus *Anopheles*; more particularly a subspecies or variant of the species *An. gambiae.*

The present disclosure is also preferably applied to dealing with a species or subspecies of mosquito of the genus *Aedes;* more particularly *Aedes aegypti.*

The present disclosure also provides a composition comprising δ-decalactone and/or δ-undecalactone in a cream, lotion, ointment, spray, gel or solid vehicle suitable for topical application to human or animal or on clothing as carrier material, such as textile fabrics. In preferred compositions there is at least 1% (w/w) δ-decalactone and/or δ-undecalactone.

The present disclosure further provides a composition for making articles such as bed nets and screens comprising δ-decalactone and/or δ-undecalactone in a synthetic resin. The resin may be extrudible or mouldable into the desired articles. The present disclosure therefore includes an extrudible or mouldable material containing δ-decalactone and/or δ-undecalactone. Any articles of utililty may be made from such resins containing δ-decalactone and/or δ-undecalactone so that they may have insect repelling effect. The concentration of δ-decalactone and/or δ-undecalactone in the resin is such that a resultant article preferably comprises at least about 1% (w/w) δ-decalactone and/or δ-undecalactone.

The present disclosure includes a fabric, textile, mesh or net, coated and/or impregnated with δ-decalactone and/or δ-undecalactone. Such fabric, textile, mesh or net may be made from natural or synthetic material. The coating and/or impregnation may be carried out after the formation of the material, or after the making of articles from the material. The articles made of fabrics or textile may be items of clothing. The meshes or nets may be bed nets. In preferred embodiments, the finished articles may be coated or impregnated so that they comprise at least about 1% (w/w) δ-decalactone and/or δ-undecalactone.

The present disclosure also provides insect repellent apparatus comprising a container containing a composition comprising δ-decalactone and/or δ-undecalactone. The container may be in fluid connection with an orifice which can be exposed to the air, or a porous surface which can be exposed to the air.

In some examples, the container and orifice provide discharge of composition into the air; optionally wherein the container containing the composition is pressurised. Most preferably the apparatus is in the form of an aerosol device and the composition includes a suitable propellant as hereinbefore described.

In other examples, the insect repellent apparatus has a porous surface from which a composition of the invention evaporates the δ-decalactone and/or δ-undecalactone active agents into the air. Optionally, at least a portion of the porous surface is heated.

The present disclosure also includes a kit comprising a first container containing a composition comprising δ-decalactone and/or δ-undecalactone, and in a second, spatially separate container an insect attractant composition optionally combined with trapping and/or killing device. The first and second containers may be in the form of any of the repellent apparatus or repellent devices described herein.

Accordingly, the present disclosure also provides a push-pull system of insect control comprising insect repellent apparatus or device as described herein, and a spatially separate insect attractor, trap or killer. Such attractors, traps or killers are well known to a person of skill in the art and are readily available from a wide range of commercial suppliers. For example, commercially available attractant mosquito traps are produced by Biogents AG, Regensburg, Germany; or Bioquip of California, USA.

The present disclosure includes a method of controlling insects in an area, comprising releasing δ-decalactone and/or δ-undecalactone at one or more locations in and/or outside of the area. Preferably, the δ-decalactone and/or δ-undecalactone is released directly into the air.

In further examples of this method of the present disclosure, one or more insect attractors, traps or killers may be located in and/or outside of the area, the insect attractors, traps or killers being at spatially separate locations from the release of δ-decalactone and/or δ-undecalactone in and/or outside of the area.

In other methods in accordance with this aspect, the δ-decalactone and/or δ-undecalactone may be released inside the area and the insect attractors, traps or killers are located outside the area.

As will be appreciated, the present disclosure therefore offers complete flexibility in terms of providing optimal push-pull insect management system for any given situation in the field.

The present disclosure will now be described in detail with reference to examples and having regard to the drawings in which:

BRIEF DESCRIPTION OF DRAWINGS

Figure 1 shows a perspective and schematic view of the apparatus used for candidate repellent bioassay.

Figure 2 is a chart showing the effect of a selection of compounds on the number of landings made by a group of *Anopheles gambiae s.s.* females during eight minutes.

Figure 3 shows the experimental setup for example 2.

CLAIMS

1. An insect repellent composition comprising δ-decalactone and/or δ-undecalactone wherein the δ-decalactone and/or δ-undecalactone is formulated for topical application to a human or animal.

2. A composition as claimed in claim 1, wherein the composition is a cream, lotion, ointment, spray, gel, solid, semi-solid or liquid; preferably wherein the δ-decalactone and/or δ-undecalactone is at a concentration of at least 1% (w/w).

3. A composition as claimed in claim 1 or claim 2, wherein the insect is a blood sucking dipteran, preferably a mosquito; most preferably a mosquito (a) of the genus *Anopheles*; preferably a mosquito of the species *An. gambiae*; or (b) of the genus *Aedes*; preferably a mosquito of the species *A. aegypti*; or (c) of the genus *Culex*.

4. A composition as claimed in any preceding claim comprising δ-decalactone and δ-undecalactone.

5. A composition as claimed in any preceding claim, wherein the δ-decalactone and/or δ-undecalactone is used in combination, separately, sequentially or simultaneously, with a further insect repellent.

6. A composition as claimed in claim 4, wherein the further insect repellent is selected from 6-methyl-5-hepten-2-one (6MHO), linalool (LNL), N,N-diethyl-meta-toluamide (DEET) and *p*-Menthane-3,8-diol (PMD).

7. An insect repellent composition for making articles, fabric, textile, mesh or net comprising δ-decalactone and/or δ-undecalactone in the form of a synthetic resin; preferably wherein the δ-decalactone and/or δ-undecalactone is at a concentration of at least 1% (w/w).

8. An article or a material coated and/or impregnated with δ-decalactone and/or δ-undecalactone; preferably at least 1% (w/w) δ-decalactone and/or δ-undecalactone; and preferably wherein the article or material is selected from a fabric, textile, mesh or net.

9. An article or material as claimed in claim 8, wherein the δ-decalactone and/or δ-undecalactone is present in a vehicle.

10. An article or material as claimed in claim 9, wherein the vehicle is a solid-semi-solid or liquid; preferably wherein the vehicle is micro-encapsulated.

11. An article or material as claimed in claim 9, wherein the δ-decalactone and/or δ-undecalactone is present in the vehicle in an amount from 0.1% (v/v) to 99% (v/v).

12. An article or material as claimed in any of claims 8 to 11, wherein the δ-decalactone and/or δ-undecalactone is present in a synthetic resin.

13. An article or material as claimed in any of claims 8 to 12, wherein the article or material further comprises a further insect repellent; preferably wherein the further insect repellent is selected from 6-methyl-5-hepten-2-one (6MHO), linalool (LNL), N,N-diethyl-meta-toluamide (DEET) and p-Menthane-3,8-diol (PMD).

14. An insect repellent apparatus comprising a container containing a composition comprising δ-decalactone and/or δ-undecalactone; preferably wherein the container is in fluid connection with an orifice which can be exposed to the air, or a porous surface which can be exposed to the air.

15. An insect repellent apparatus as claimed in claim 14, wherein the container and orifice provide discharge of composition into the surrounding airspace; optionally wherein the container containing the composition is pressurised, e.g. is an aerosol.

16. An insect repellent apparatus as claimed in claim 14, wherein composition evaporates on the porous surface; optionally wherein at least a portion of the porous surface is heated.

17. Use of δ-decalactone and/or δ-undecalactone as an insect repellent.

18. A push-pull system of insect control comprising insect repellent apparatus of any of claims 14 to 16, and a spatially separate insect attractor, optionally included as part of a trap or killer.

19. A method of controlling insects in an area, comprising releasing δ-decalactone and/or δ-undecalactone into the air at one or more locations in and/or outside of the area.