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(*E*)-3-Tridecen-2-one, an antibiotic from the interdigital glands of black-tailed deer *Odocoileus hemionus columbianus*

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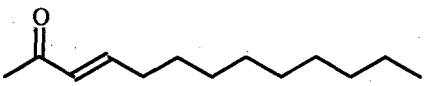
Abstract. (*E*)-3-tridecen-2-one, the major volatile component of interdigital gland extracts from the black-tailed deer, *Odocoileus hemionus columbianus*, inhibited the growth of gram-positive bacteria and fungi. The bacteria, *Propionibacterium acnes*, and the fungi, *Trichophyton mentagrophytes* had a minimum inhibitory concentration (MIC) of 12.5 μg/mL and 25 μg/mL, respectively.
Key words. Black-tailed deer; *Odocoileus hemionus columbianus*; (*E*)-3-tridecen-2-one; antimicrobial activity; interdigital gland.

Interdigital glands are found in the feet of most species of the deer and antelope. It has long been speculated that the primary function of interdigital glands secretion is to mark the ground where the animal has passed[1]. The chemicals secreted from these glands have been described for only two species, the reindeer, *Rangifer tarandus tarandus*[2–5] and an African antelope, the bontebuck, *Damaliscus dorcas dorcas*[6,7]. The compounds identified from reindeer interdigital glands are 1-hydroxy-7-methyl-3-octanone, 7-methyl-1-octen-3-one, 7-methyl-3-octanone and 6-methyl-2-heptanone and eight short-chain carboxylic acids. Reindeer actively investigate interdigital gland secretion of conspecifics[8] but only respond to two of the components, isobutyric and isovaleric acids[3]. The major volatile constituent of this gland from the bontebuck is (*Z*)-5-undecen-2-one. Minor components from this gland are 2-heptanone, 2-nonanone, 2-undecanone, 2,5-undecanedione, α-terpineol, 2-heptylpyridine, *m*-cresol, and (*Z*)-6-dodecen-4-olide. Limited response to interdigital gland secretion from conspecifics or to individual components of this secretion was reported for the bontebuck[9].

Black-tailed deer (*Odocoileus hemionus columbianus*) are a subspecies of mule deer that inhabits the Pacific coastal mountain ranges of North America from central California to central British Columbia. This deer has well developed interdigital glands in fore- and hind-feet. An unctuous secretion covers the inner surface and hair in these glands and stains the hair on the dorsal surface of the foot. Müller-Schwarze did extensive studies on pheromones of black-tailed deer but found no behaviour associated with deer smelling the hoof prints of conspecifics[10].

Gas chromatographic-mass spectral analysis of an ether extract of this secretion from 5 males and 3 females showed the same major volatile compound. The mass spectra of this compound is m/z = 196(M^+, 2), 181(8), 97(31), 96(14), 83(22), 81(20), 71(34), 69(31), 55(65), 43(100), 41(44). The molecular ion at m/z = 196 suggested a compound with a molecular formula of $C_{13}H_{24}O$ and two sites of unsaturation. The base peak at m/z = 43 (CH_3–CO–) indicated one site of unsaturation is due to a methyl ketone. A fragment at m/z = 69 (CH_3–CO–CH = CH–) implied that a double bond is adjacent to the ketone. A possible candidate compound, 3-tridecen-2-one (**1**) was synthesized[11] and found to



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have identical gas chromatographic retention time and mass spectrum as the major compound in the gland. The synthetic sample of 3-tridecen-2-one was shown to be the (*E*)-isomer by the ^{1}H-NMR coupling constant of 15.9 Hz for the olefinic protons and an IR absorption at 980 cm^{-1}. The spectral properties of this liquid are, 300 MHz ^{1}H-NMR δ ($CDCl_3$) 6.81(dt, 1H, J = 15.9 Hz, 6.9 Hz), 6.06(dt, 1H, J = 15.9 Hz, J = 1.48 Hz), 2.24(s, 3H), 2.22(quart, 2H), 1.46(m, 2H), 1.26(m, 12H) and 0.88(t, 3H); 75 MHz ^{13}C-NMR δ ($CDCl_3$) 198.80, 148.69, 131.24, 32.47, 31.85, 29.46, 29.37, 29.27, 29.17, 28.07, 26.79, 22.65, and 14.09; and FT-IR (neat) 2925, 2854, 1700, 1677, 1628, 1467, 1360, 1253, 1189 and 980 cm^{-1}. No 3-tridecen-2-one was seen in ether extracts of hair removed from the leg above the interdigital gland, indicating the source of the compound is the interdigital gland.

Since Müller-Schwarze studies on black-tailed deer showed no behaviour associated with interdigital gland secretion[10], we investigated possible antimicrobial activ-

ity of (*E*)-3-tridecen-2-one against various bacteria, yeast and fungi[12]. It showed activity [minimum inhibitory concentration (MIC)] against the gram-positive bacteria *Bacillus subtilis* (100 μg/mL), *Brevibacterium ammoniagenes* (100 μg/mL), *Staphylococcus aureus* (50 μg/mL), *Streptococus mutans* (25 μg/mL), and *Propionibacterium acnes* (12.5 μg/mL). This compound was not active (MIC > 800 μg/mL) against the gram-negative bacteria, *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Escherichia coli*, and *Proteus vulgaris*. Activity against yeast was mixed, no activity (MIC > 800 μg/mL) was seen against *Saccharomyces cerevisiae* and *Candida utilis*, although *Pityrosporum ovale* showed *moderate* inhibition (MIC, 100 μg/mL). Moderate activity was seen with the fungus *Penicillium chrysogenum* (MIC, 400 μg/mL), while the fungus *Trichophyton mentagrophytes* was strongly inhibited at 25 μg/mL. *T. Mentagrophytes*, the organism responsible for athlete's foot in humans, infects a number of animal species.

Antibiotic lipids have previously been identified from the skin of animals. These compounds are fatty acids and their monoglycerol esters,[13,14] and glycerosphingolipids and phospholipids[14]. (*E*)-3-Tridecen-2-one represents a new class of lipid antibiotics found on animal skin. The speculation that the function of ungulate interdigital gland secretion is used primarily for semiochemical marking may need to be reinvestigated. The major function of this gland might be to secrete antimicrobial substances that keep microorganisms from attacking the feet, hooves or other body areas. It is also possible that in many cases, interdigital gland compounds may serve the dual function as semiochemical markers and antibiotics.

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