ABSTRACT

Algorithms for classification and taxonomy based on criteria as information entropy and its production are proposed. Some local anaesthetics, currently in use, are classified using five characteristic chemical properties of different portions of their molecules. Many classification algorithms are based on information entropy. When applying the procedures to sets of moderate size, an excessive number of results appear compatible with data and the number suffers a combinatorial explosion. However, after the equipartition conjecture one has a selection criterion between different variants resulting from classification between hierarchical trees. Information entropy and principal component analyses agree. A table of periodic properties of anaesthetics is obtained. The first three features denote the group while the last two indicate the period in the table. The anaesthetics in the same group and period are suggested to present maximum similarity in properties. Furthermore the ones with only the same group will present important resemblance.
1. INTRODUCTION

Most analgesics–anaesthetics used today are tertiary–secondary amines that at physiological pH are cationic (alfentanil, bupivacaine, butorphanol, chloroprocaine, cocaine, codeine, dyclocaine, fentanyl, ketamine, lidocaine, meperidine, mepivacaine, morphine, nalbuphine, prilocaine, sufentanil, tetracaine) (Matsuki et al., 1997). There are also the intravenous anaesthetics brevital (methohexital sodium) and diprivan (propofol), and the topical analgesic zostrix (capsaicin) that have the capacity to contain anionic (phenolate) species (Frangopol & Mihâilescu, 2001). In addition to being able to carry a charge the drugs exhibit substantial hydrophobic character, i.e., contain ionisable–nonpolar moieties. They are exactly the types of molecular species, the sustained release of which can be most effectively achieved by transductional protein-based polymers. With the emergence of new laser–surgical techniques the need for more effective topical anaesthesia grows. Several topical local anaesthetics are being used before various dermatologic procedures. The EMLA is the most commonly used agent; however several new topical anaesthetics claimed increased efficacy and faster onset of action. Topical anaesthetics are weak bases typically constructed of three important components: an aromatic ring, intermediate-length ester–amide linkage and tertiary amine. The ester anaesthetics have an ester linkage, while amide anaesthetics have an amide linkage between the aromatic ring and intermediate chain. Ester-type topical anaesthetics are metabolized by plasma cholinesterase and other non-specific esterases, while amide anaesthetics are primarily metabolized in the liver via microsomal enzymes. Allergic contact reactions to the ester group of anaesthetics are common while amide anaesthetics (lidocaine, prilocaine) are rare sensitizers (Suhonen & Kanerva, 1997). The metabolite p-aminobenzoic acid (PABA), formed by ester hydrolysis, is capable of causing allergic reactions in a small percentage of patients (Mackie & Mackie, 1999). Ester-linked anaesthetics are contraindicated in patients with allergies to PABA, hair dyes and sulphonamides. Topical anaesthetics prevent the initiation–transmission of nerve impulses and provide cutaneous analgesia by targeting free nerve endings in the dermis. Topical anaesthetics block nerve impulse conduction by interfering with the function of Na+ channels. By inhibiting Na+ flux the threshold for nerve excitation increases until the ability to generate an action potential is lost. The stratum corneum is the main barrier to topical anaesthetic delivery (Adriani & Dalili, 1971). Seeman (1972) reviewed the membrane actions of anaesthetics–tranquilizers. The most general definition of an anaesthetic is a drug which, when applied directly to the nerve or muscle cell, reversibly blocks the action potential without appreciable affecting the resting membrane potential of the cell. According to the definition, a wide variety of lipid-soluble compounds are anaesthetic, e.g., tranquilizers, anticonvulsants, antihistamines, steroids, detergents, anti-arrhythmics, narcotics, vasodilators and sedatives (cf. Figure 1).

The aromatic portion of anaesthetic molecules is primarily responsible for the lipid solubility, which allows diffusion across the nerve cell membrane (cf. Figure 2) determining the intrinsic potency of agents (Covino, 1972, 1980, 1986). Aromatic–amine portions determine protein-binding characteristics, which are the primary determinant of anaesthesia duration.

Different methods for evaluating anaesthetic efficacy include venipuncture, pinprick testing, split-thickness skin graft donation and laser pulses as pain stimuli. Laser-induced thermal pain stimuli are advantageous for comparing topical anaesthetics by providing reproducible, quantifiable stimuli with minimal intraindividual variation. The pulses also provide selective activation of nociceptors without interference from mechano-sensitive receptors. The drugs exist in cationic–uncharged forms under normal in vivo conditions. The most important clinical properties of local