SAFFAN®: A REVIEW AND SOME EXAMPLES OF ITS USE IN FISHES (PISCES: TELEOSTEI)

by

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ABSTRACT

Saffan®, previously known as CT1341, is an injectable steroid anesthetic for use in cats and monkeys. It is also suited to induce anesthesia in fishes. It has the convenient property to induce anesthesia of the central nervous system, and to leave the sensory system of the integument operational. The active constituents are alphaxalone and alphadolone. A dose of 24 mg/kg i.m. is sufficient for 2 to 3 hours narcosis in fish of several hundreds of grams. For small specimens administration via bath-water in doses of 2 to 4.8 mg/l for induction and half this dose for maintenance are advisable. In catfish, Ictalurus nebulosus and I. melas, of 100 g or more the induction time after i.m. injection with 21 mg/kg is about 20 min and independent of weight or temperature. The recovery time varies with temperature from 213 min at 13°C to 19 min at 19°C. In 1000 g catfish, Clarias gariepinus, the onset of surgical anesthesia occurs after 26 min on average at doses of 24 mg/kg at 24°C. In 5 g catfish, Kryptopterus bicirrhis, 4.8 mg/l bath water at 25°C makes the opercular movements disappear after 5 min. For 15 cm TL Gnathonemus petersii a good induction dose is 2 mg/l bathwater. After 20 minutes at 23°C surgical narcosis is reached.

KEY WORDS: Alphaxalone/alphadolone acetate, Alphathesin®, Althesin®, chemoreception, Clarias, CT1341, electroreception, Gnathonemus, Ictalurus, Kryptopterus, Saffan®.

INTRODUCTION

The first report on steroids possessing anesthetic potencies came from SELYE (1941), who injected rats with steroid hormones in order to unravel their physiology. Desoxycorticosterone and progesterone proved to be most potent. The difficulty with steroids as anesthetic agents is that they are water-insoluble. Laubach and colleagues (LAUBACH et al., 1955) overcame this adversity by developing the water-soluble hydroxydione by esterification of the 21-hydroxy derivative of pregnanedione. Hydroxydione has a high therapeutic index (17.3), but also several disadvantages, namely a slow induction and a high incidence of irritation at the site of

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1 LD50 / AD50: the lethal-dose/anaesthetic-dose, each for 50% of the test animals.

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injection and of the veins (SEAR, 1995). Eventually Glaxo CT1341 was
developed. CT1341 has an even higher therapeutic index (30.6) than hy-
droxydione, shows fast induction, and is non-irritant (CHILD et al., 1971).
CT1341 was marketed as Saffan® for veterinary use and as Alfathesin®
(BROGDEN et al., 1974) or Althesin® (CORNET & POPESCU, 1977) in
human clinical practice. Experiments on fish showed that Saffan® does
not block the neuromuscular synapse in trout (OSWALD, 1978) and leaves
the spontaneous activity of electroreceptor organ primary afferents in cat-
fish intact (PETERS & IEPEREN, 1989; PETERS et al., 1997a; 1997b).
Apparently it depresses mainly the activity of the central nervous system.
This feature makes it a very valuable drug for research in sensory physi-
ology, where it can be used for immobilisation. In this way Saffan® has
also been used successfully in mechanoreceptor research in fish (RUSSEL
& LOWE, 1983; VAN NETTEN & KROESE, 1987; KROESE & VAN NET-
TEN, 1987; KROESE & SCHELLART, 1992) and in chemoreception re-
search (RESINK et al., 1989).

Hereafter we present a brief review on the properties of Saffan®,
exemplified by some data from experiments on fish.

REVIEW

Anesthetic steroid components of Saffan®

The components of Saffan® are the steroids alphaxalone (3alpha-hydroxy-
5alpha-pregnane-11,20-dione, 9 mg/ml; fig. 1A) and alphadolone acetate
(21-acetoxy-3alpha-hydroxy-5alpha-pregnane-11,20-dione, 3 mg/ml; fig.
1B). The anesthetic potency of alphaxalone is twice the potency of al-
phadolone acetate; the anesthetic potency of the mixture (Saffan®) is con-
sistent with the addition of activities of its components. Both steroids are
hydrophobic and therefore solubilised in saline by 20% w/v Cremophore
EL (polyoxyethylated castor oil). The concentration of the active compo-
nents in the solubilised saline is 1.2% w/v. Alphadolone is added to in-
crease the solubility of alphaxalone (ROSS & ROSS, 1983; SEAR, 1995).

Anesthesia

The general idea on anesthesia is that either excitatory transmission is
depressed, inhibitory transmission is enhanced, or that both occur simul-
taneously. One of the first observations on the effects of alphaxalone (and
of other general anesthetics) revealed a prolonged inhibition of neurones
in the guinea pig olfactory cortex (SCHOLFIELD, 1980). The following