

## Trends towards the use of natural anesthetics in fish

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### Review Article

Volume: 6, Issue: 1  
April 2022  
Pages: 42-46

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### ABSTRACT

Anesthesia is generally defined as the loss of sensation caused by a pharmacological agent resulting from the suppression of the nervous system. Anesthetic agents are used to reduce stress, facilitate surgical operations requiring prolonged immobilization, in transportation, classification, handling, sorting, tagging, grading, weighing, measuring or vaccination in fish. In order to talk about an adequate level of anesthesia, signs such as loss of balance, relaxation in muscle tone, decreased respiration and inability to respond to stimuli must be observed in the fish. A good anesthetic agent must not have toxic side effects, be able to be eliminated from the body in a short time, not have permanent physiological, immunological or behavioral effects. In order to determine the optimal anesthesia dose, exposure time and maximize the drug's efficacy in fish, the size of the fish and the characteristics of the water it is in need to be determined beforehand. There are two types of commercial anesthetics, natural and synthetic. Although chemical anesthetics are commonly used for fish, there has been a recent trend towards the use of natural anesthetics due to safety, residue problems, accumulation in the fish body and side effects. These new herbal anesthetics have more favorable properties for the health of both fish species and the people who consume them.

### Article History

Received: 16.03.2022  
Accepted: 13.04.2022  
Available online:  
30.04.2022

DOI: <https://doi.org/10.30704/http-www-jivs-net.1089008>

To cite this article: Yaşar, T. Ö., Yardımcı, M. (2022). Trends towards the use of natural anesthetics in fish. *Journal of Istanbul Veterinary Sciences*, 6(1), 42-46. **Abbreviated Title: J. İstanbul vet. sci.**

## Introduction

Anesthesia is the suppression of the functions of a part or whole of the body due to loss of sensitivity by a natural or synthetic pharmacological agent (Aktop et al., 2019). Anesthetic drugs can be used for sedative, reducing stress and struggle, minimizing physiological changes, rendering them amenable to handling during invasive procedures such as blood sampling or injection and for euthanasia in fish (Aktop et al., 2019;

Neiffer and Stamper, 2009; Rairat et al., 2021). Most fish encounter anesthetic agents at some point in their lives for the reasons stated above (Readman et al., 2013).

Due to the potential harms of chemical anesthetics, the interest in herbal anesthetics in aquaculture is increasing day by day (Can and Sümer, 2019). Herbal anesthetics are considered safe agents

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due to their natural ingredients, not causing any side effects, not having carcinogenic properties and not accumulating in tissues (Aktop et al., 2019).

The aim of this study is to compare and evaluate chemical anesthetics and natural anesthetics used in fish.

There are about 30,000 different fish species. Teleosts account for almost 96% of this. For this reason, most anesthesia studies are performed with teleosts. To a lesser extent, sharks, elasmobranchs such as stingrays, and other fish species are used in these studies. There are anatomical, physiological and behavioral differences between fish breeds. Given these differences, extrapolation of limited data on the anesthetics used could potentially carry risks. It provides a better understanding of anesthetic agents developed on unknown fish breeds and drug combinations, and their natural history and taxonomic relationship. (Neiffer and Stamper, 2009).

**Properties of a good anesthetics in fish:** In the selection of an ideal anesthetics for fish, some of the most important criteria to be considered are to be easy to use, not to be toxic or harmful living things and the environment, to be economical, having a rapid induction with quick excretion and recovery and not producing residues (Hamackova et al., 2006; Schroeder et al., 2021). The optimal dose of a fish anesthetic depends on species, fish size, environmental factors and process to perform (Javahery et al., 2012). The time for the fish to enter anesthesia should not exceed 3 minutes, and the time for exit from anesthesia should not exceed 5 minutes. It should show sufficient effect at low doses. It should be low cost and easily available (Aktop et al., 2019).

In general, the anesthesia phase should be short, and loss of balance and muscle tone in the fish should occur rapidly for handling (measuring, vaccination, grading) and the recovery stage should be calm and rapid (Bodur et al., 2018). Recovery from anesthesia can be observed when fish are returned to non-medicated water. Main signs are operculum movement and motions of swimming and balance (Schroeder et al., 2021).

**Comparison of chemical and natural anesthetic agents:** Commonly used synthetic anesthetics in fish are MS-222 (Tricaine methane sulfonate), benzocaine, isoeugenol, AQUI-S, 2-phenoxy ethanol, metomidate, quinaldine and carbon dioxide. The recommended induction and recovery time of less than 5 minutes for good anesthesia is among the

values close to synthetic anesthetics in natural anesthetics (Husen et al., 2014; Purbosaria et al., 2019; Sneddon, 2012)

Essential oils of different plants such as Lamiaceae, Verbenaceae, Lau-raceae and Myrtaceae are mainly studied in order to benefit from their anesthetic effects in fish. In addition to these, herbal compounds such as menthol, linalool, myrcene, cineole, globulol, spathulenol, guaial, caryophyllene oxide, terpinen-4-ol and dehydrofuquinone have been investigated for their anesthetic effects in recent years (Hoseini et al., 2019; Can and Sümer, 2019).

Clove oil is an effective, local and natural anesthetic that is widely used in fish today (Javahery et al., 2012). It is obtained by distillation of the flowers, stems and leaves of the clove tree *Syzygium aromaticum* (Husen and Sharma, 2014). Clove oil is less expensive and more cost-effective than MS-222, a chemical anesthetic. Oregano and eucalyptus oils are also inexpensive products like clove oil (Bodur et al., 2018). In fact, it can be said that Clove oil and eugenol are relatively more effective natural anesthetic agents compared to synthetics in terms of induction and recovery times (Purbosaria et al., 2019). The disadvantage of clove oil as an anesthetic is that its dosage is sensitive during application. A small variation in dosage can result in fish death or slow recovery time (Kamble et al., 2014).

Another example of essential oil that has been studied is coriander oil (*Coriandrum sativum*), which is derived from coriander mot. Coriander contains the active ingredient linalool, which is anesthetized in 50-70% of the main components. Depending on whether it is dry or wet, the essential oil content of coriander (*C. sativum* L.) fruits varies between 0.03-2.60% and is used for anesthetic purposes in fish (Aktop et al., 2019; Can et al., 2019).

*Ocimum gratissimum* was also found to be an effective and safe anesthetic in fish (Silva et al., 2012). It is commonly known as alfavaca or tree basil. It is often used as a spice and is also used as a sedative and cure for stress and headaches in human medicine (Albuquerque et al., 2007).

Linalool and myrcene are other substances used in fish anesthesia (Mirghaed et al., 2016). Citronellal anesthetic activity is higher than linalool and lower than eugenol. However, it can be preferred in terms of fish health as it causes less tissue problems (Yousefia et al., 2018).

Lavender essential oil has been found to be

effective in anesthetizing fish similar to clove extract without any side effects (Raisi et al., 2020).

Tricaine methanesulfonate (MS-222) is a synthetic agent frequently used in fish anesthesia (Pubosari et al., 2019; Harmon, 2009). However, tricaine methanesulfonate (MS-222) has been reported to have pharmacokinetic and pharmacodynamic differences in its substance (Topic et al., 2012). It has also been reported that this compound has a repulsive negative effect for some fish species (Readman et al., 2017). Other studies have shown that MS-222 may cause state changes in the immune system and biochemical parameters such as increased cortisol, and altered oxidative and immune responses in different fish species during transport (Cao et al., 2019, Kenter et al., 2019).

A number of studies have been conducted on the effects of anesthetics such as propofol (2,6-diisopropyl phenol), a GABA A agonist that is widely used for human and veterinary anesthesia, in different fish species (Fleming et al., 2003, Gressler et al., 2015). Propofol was reported to be a short-acting, rapid healing, and rapidly metabolized anesthetic agent without cumulative effects in a study conducted with the Nile tilapia (*Oreochromis niloticus*) species (Valença-Silva et al., 2014). Due to between- and within-species drug responses differences, anesthetics must be investigated on a species-by-species basis to assure its safe use (Toutain et al., 2010). At the end of transport in a study, propofol increased glucose levels while decreasing hematocrit (HCT) and lactate levels. Compared to naïve animals, animals carried with MS-222 had decreased levels of HCT and lactate, while cortisol levels increased. Cortisol levels were also increased in the control animals and were still elevated 24 hours later. In addition, there was a decrease in gill ROS levels and GST activity after transport with propofol compared to the control group. However, fillet quality and histopathology of the gills did not change in all tested groups (Félix et al., 2021).

**Use of high-dose anesthetic for euthanasia :** Overdose of immobilization drugs can be used for fish euthanasia (AVMA 2007). The most commonly preferred option for fish euthanasia is the use of immersion drugs (especially MS-222) between five and ten times the anesthetic concentrate for a given species. However, injectable agents are also effective (Ross and Ross, 1984). In large fish breeds, immersion and bathing method is not appropriate

and practical. Dipping medicine for fish is poured directly over the gills. (Harms and Bakal 1995). With the exception of some breeds, generally keeping the fish in the anesthetic solution for 5 to 10 minutes after the cessation of opercular movement is sufficient for euthanasia. Fish myocardial cells do not need blood sugar for energy and use local glycogen stores. Therefore, cardiac asystole typically lags behind brain death (Stetter 2001). Doppler probes, ultrasonography, or electrocardiography may be used to confirm cardiac asystole. In addition, intravenous (in the heart or caudal vein) anesthetic drug or pentobarbitone administration can be done to ensure cardiac asystole (Ross 2001). Spinal transection or cranial concussion, blood loss applications are also alternative methods in deeply anesthetized fish (Harms 1999). Although the effectiveness of using carbon dioxide for immobilization has been reported, it is difficult to control concentrations of this substance in water. It is also known to have negative effects on oxygen levels, blood gases, and acid-base balance. (Gelwicks and Zafft 1998; Harms 1999; Prince et al. 1995).

## Conclusion

Since compounds that are aversive in fish anesthesia cannot be routinely used in practice, herbal anesthetics play a key role as alternative. It is known that there are about thirty thousand fish breeds. It is impossible to perform anesthesia studies on all fish breeds. However, using as many different types and anesthetic agents as possible will increase the knowledge and experience in this matter. In line with the studies and results obtained, it has been reported that MS-222, a synthetic agent frequently used in fish anesthesia, may endanger the health and welfare of fish. It is reported that anesthetics of natural origin have a more positive effect on welfare during fish transportation. However, more research is needed to clarify this situation in the light of developing technology and information.

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