CHAPTER 1

Fish-Induced Keriorrhea

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Contents

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Abstract

Many deep-sea fishes store large amounts of wax esters in their body for buoyancy control. Some of them are frequently caught as by-catch of tuna and other fishes. The most noteworthy ones include escolar and oilfish. The accumulation of the indigestible wax esters in the rectum through consumption of these fish engenders discharges or leakage *per rectum* as orange or brownish green oil, but without noticeable loss of water. This physiological response is called keriorrhea, which is variously described as "oily diarrhea," "oily orange diarrhea," or "orange oily leakage" by the mass media and bloggers on the internet. Outbreaks of keriorrhea have been repeatedly reported across continents. Additional symptoms including nausea, vomiting, abdominal cramps, and diarrhea were complained by the victims. They are probably due to anxiety or panic when suffering from keriorrhea. Escolar and oilfish are banned from import and sale in Italy, Japan, and South Korea. Rapid detection of the two fishes is imperative to ensure proper labeling and safeguarding of the public before and after any keriorrhea outbreak.

I. INTRODUCTION

A. Fish as food

Fishes are an excellent source of proteins, polyunsaturated fats, vitamins, and other nutrients. The wide range of biodiversity in fishes allows a good selection of different forms, sizes, colors, tastes, and textures to fit one's diet preferences. When served alone or in combination with various spices, other meats, and vegetables, and prepared by a range of culinary methods, there are unlimited ways to turn fish into the most enjoyable gourmet item. As compared to other sources of meat, consumption of fish has additional health benefits, which is most often associated with the presence of omega-3 long-chain ($>C_{20}$) polyunsaturated fatty acids (ω3 LC-PUFA). This provides protection against cancer of the alimentary tract, coronary heart diseases, stroke, and other disorders (Erkkila *et al.*, 2004; Fernandez *et al.*, 1999; He *et al.*, 2004; Hu *et al.*, 2002; Mozaffarian and Rimm, 2006; Norat *et al.*, 2005).

Fishes may also occasionally cause harm to health. When incompletely cooked or improperly handled, fishes can become a medium for transmission of parasites and diseases (Butt *et al.*, 2004a,b). Allergens such as parvalbumins in fish muscles or even parasites such as *Anisakis simplex* in fish can cause allergic reactions (Du Plessis *et al.*, 2004; Lehrer *et al.*, 2003; Poulsen *et al.*, 2003; Taylor *et al.*, 2004; Wild and Lehrer, 2005). The safety of fish consumption is now a major consumer worry (Brewer and Prestat, 2002; Lyon, 2008; Senkowsky, 2004; Verbeke *et al.*, 2008) and the news of poisoning after fish consumption is not infrequent. Certain components in fish including tetrodotoxin and ciguatera toxins are notorious for their toxic properties (Hashimoto and Fusetani, 1978; Kazuo, 1999; Lawrence *et al.*, 2007; Lehane and Lewis, 2000; Miyazawa and Noguchi, 2001; Noguchi and Ebesu, 2001; Stommel and Watters, 2004; Ting and Brown, 2001). Mercury and other heavy metals and various contaminants, such as pesticides, other organochlorines, and antibiotics, accumulated in fish are a serious concern (Du Plessis *et al.*, 2004; Guallar *et al.*, 2002; Hightower and Morre, 2003; Kostyniak *et al.*, 1998; Senkowsky, 2004).

A common response to fish poisoning is diarrhea, often in the form of loose and watery stools accompanied with excessive water loss. However, in some special cases, the uncontrollable urge of bowel movements and discharges do not involve a noticeable loss of water. In those cases, oil is discharged or leaked through the rectum, and this type of poisoning responses is called keriorrhea or keriorrhoea.

B. Keriorrhea

Keriorrhea specifically refers to the pathological symptom of involuntary passage or leakage of oil, or actually wax esters, through the rectum. This term was coined by Berman *et al.* (1981) based on the Greek words *keri* and *diarroia*, which mean ''wax'' and ''to flow through'', respectively. More specifically, they refer to the symptoms observed in cases developed after consumption of certain oily fish, wherein the oil discharged appears orange or brownish green in color, while little water is lost (Fig. 1.1). This ailment is variously described as ''oily diarrhea'', ''oily orange diarrhea'', or ''orange oily leakage'' by the mass media and bloggers on the internet.

C. Case reports and symptoms

Outbreaks of keriorrhea have been reported in many continents, including Africa, America, Asia, Australia, and Europe (Table 1.1). However, few are recorded in the scientific or medical literature. Therefore, the

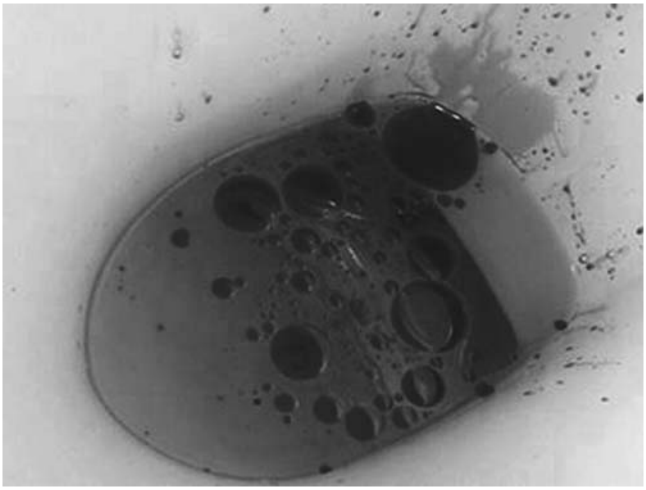

FIGURE 1.1 Oil discharged after consumption of escolar. Reprinted with permission from Ruello (2004, Nick Ruello of Ruello and Associates Pty Ltd.).

actual number of affected people over the years are largely underestimated as the internet is floating with many more reports or communication about personal experiences of embarrassing oily diarrhea after consumption of fish. In most cases, these fishes came into the spotlight because of a large outbreak that involved a substantial number of people; otherwise, scattered occurrences are generally neglected.

Australia has documented several keriorrhea outbreaks, allowing further tracing into the etiology and symptoms in patients. In South Australia, between 1997 and 1999, there were nine cases of gastrointestinal complaints after rudderfish consumption. In two episodes that took place in 1999, patients complained of diarrhea, often oily and orange colored, within hours of consumption. Through protein fingerprinting, the implicated fish was identified as escolar (Givney, 2002).

Two outbreaks of diarrhea in 1999 and 2001 were reported to be associated with butterfish consumption in Victoria, Australia. The victims complained of diarrhea or yellow oily diarrhea. The fish causing the outbreaks in 1999 was identified as either escolar or rudderfish, and the one in 2001 as escolar (Gregory, 2002)

Another outbreak of gastrointestinal illness occurred among attendees of a conference lunch in New South Wales, Australia, in October 2001. Analysis of the oil in the fish samples served revealed a high proportion of wax ester (96–97%) and showed close resemblance to the oil composition in escolar. A distinctive symptom reported by many ill persons was the presence of oily diarrhea. Investigators of the outbreak conducted a

TABLE 1.1 Selected cases of keriorrhea outbreak related to escolar and oilfish consumption

Fish involved	Location	Date	No. of people affected	Remarks	References
Oilfish	South Korea	May 2007	N/A	White tuna sushi at restaurants	Fuga (2007)
	Toronto, Canada	February 2007	N/A	Mislabeled as cod or sea bass	CBC (2007); Jacquet and Pauly (2008)
	Hong Kong SAR, China	January 2007	600+	Mislabeled as cod	*Ling *et al.* (2008a,b); Jacquet and Pauly (2008)
	Victoria, Australia	August 2001	5	Mislabeled as butterfish	**Gregory (2002)
	Sydney, Australia	January 2001	9	Fish curry in a canteen	Leask *et al.* (2004)
	Victoria, Australia	November 1999	11	Mislabeled as butterfish	**Gregory (2002)
	Victoria, Australia	November 1999	~10	Mislabeled as butterfish	**Gregory (2002)
Escolar	California, USA	11 August 2003	42	Served in a buffet	Feldman *et al.* (2005)
	New South Wales, Australia	October 2001	20	Mislabeled as rudderfish or butterfish	Yohannes *et al.* (2002)
	South Australia	October 1999	N/A	Mislabeled as rudderfish	Givney (2002)
	Cape Town, South Africa	1989	N/A	Mislabeled as rudderfish	Berman *et al.* (1981)

* Escolar could be possibly involved in a few cases.
** The fish involved were reported as escolar but under the scientific name *Ruvettus pretiosus*.

telephone interview of the cohort of conference attendees using a standard questionnaire. Out of 44 attendees, 20 (46%) became ill following the conference. The median incubation period was 2.5 h (range 1–90 h). The most common symptoms reported were diarrhea (80% including 38% reporting oily diarrhea), abdominal cramps (50%), nausea (45%), headache (35%), and vomiting (25%). None of the food or beverages consumed was significantly associated with the illness. However, all individuals who consumed fish became sick, but not those who did not (four persons). Among those who consumed fish, the following potential risk factors did not have a significant association with the illness: body mass index (BMI), age, health status, and the amount of fish consumed (Yohannes *et al.*, 2002).

II. FISH INCRIMINATED

A. Escolar and oilfish

Outbreaks of keriorrhea are reported in consumers who admitted having consumed various fishes (e.g., Atlanta cod, butterfish, cod, ruddercod, or rudderfish). However, so far, almost all episodes can be traced to two varieties: escolar and oilfish.

1. Biology

Escolar and oilfish belong to the Gempylidae (snake mackerel) family in the order Perciformes (Alexander *et al.*, 2004; Nakamura and Parin, 1993). There are currently 24 species under 16 genera in Gempylidae, and they are all found in the marine environment (FishBase, 2008). All species in this family usually occur in very deep waters in tropical and subtropical seas (Nakamura and Parin, 1993). They have elongated and compressed body with isolated finlets after the anal and dorsal fins (Nakamura and Parin, 1993).

Escolar (*Lepidocybium flavobrunneum* Smith) is also called black oilfish (Fig. 1.2A and B). It is a large fish (up to 2-m long, but usually 150-cm wide) covered with small cycloid scales and smooth skin (Fishbase, 2008). It has a faint but highly undulating lateral line on the semifusiform body, which changes color from dark brown to almost black with age. In addition, a prominent keel flanked with two small oblique ridges, one on each side of the keel, is present on the caudal peduncle (Nakamura and Parin, 1993; Pauline, 1980). A single species of escolar is generally recognized. However, Brendtro *et al.* (2008) recently analyzed the mitochondrial control region and flanking tRNA sequences for 225 escolar specimens collected from six sites at different locations of the Atlantic and Pacific Oceans. Their results revealed two distinct clades, one for the

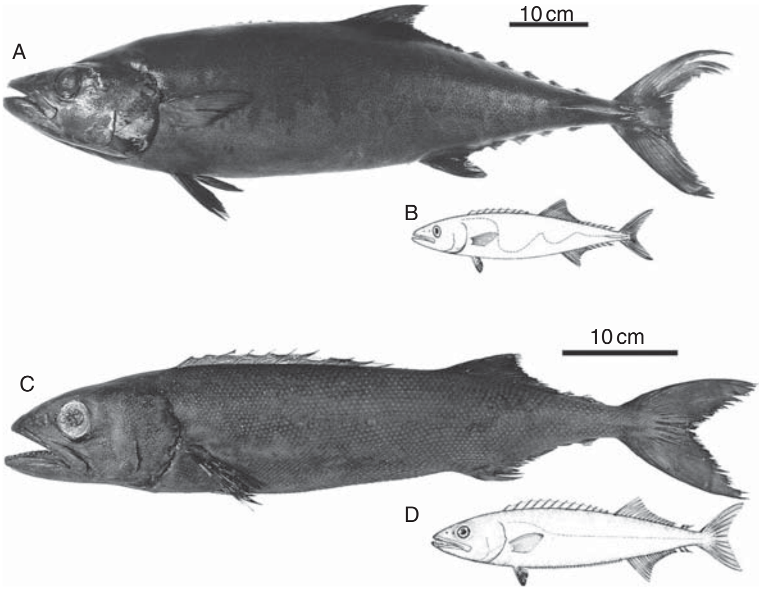

FIGURE 1.2 (A) Escolar (Regulatory Fish Encyclopedia, U.S. FDA, 1993–2008, reprinted with permission); (B) Line drawing of escolar (Nakamura, 1995, Food and Agriculture Organization of the United Nations, reprinted with permission). (C) Oilfish (Regulatory Fish Encyclopedia, U.S. FDA, 1993–2008, reprinted with permission); (D) Line drawing of oilfish (Schneider, 1990, Food and Agriculture Organization of the United Nations, reprinted with permission).

Atlantic and the other for the Pacific (plus four from South Africa) samples. A previous study by Collette *et al.* (1984), interestingly, also noted differences between escolar in the Atlantic and the Indo-Pacific regions, their vertebral counts being 31 and 32, respectively. There is a possibility that two species or subspecies of escolar may be warranted (Brendtro *et al.*, 2008).

Oilfish (*Ruvettus pretiosus* Cocco) is also called castor-oil fish (Fig. 1.2C and D). It is a large fish (up to 3-m long, but usually 100–150 cm wide) possessing a dark brown semifusiform body and a single, usually obscure, lateral line. Its lower jaw slightly protrudes beneath the upper jaw (Bettoso and Dulcic, 1999; Fishbase, 2008). Rows of spiny tubercles on the cycloid scales make the skin of oilfish very rough. A layer of porous blubber-like tissue is observed after the scales are removed (Gudger and Mowbray, 1927). In addition, a rigid and scaly abdominal keel is located on the ventral contour of the fish (Bettoso and Dulcic, 1999; Bone, 1972; Nakamura and Parin, 1993).

Escolar and oilfish are commonly found at depths between 100–800 m and 200–1100 m, respectively (Nakamura and Parin, 1993). As in many deep sea fish, both escolar and oilfish lack a swim bladder. Their buoyancy in water is achieved by the storage of large amounts of low-density lipid, particularly in the dermis, flesh, and the bones of the skull (Bone, 1972). The stored lipid provides a sufficient lift to make them neutrally buoyant. Oilfish, at rest, hangs in the water heads up at 45° to the horizontal (Bone, 1972).

2. Chemistry

Both escolar and oilfish possess considerable lipid in the body, accounting for approximately 20% of their wet weight (Cox and Reid, 1932; Gudger, 1925; Mori *et al.*, 1966c; Nichols *et al.*, 2001; Ukishima *et al.*, 1987). The major components contributing to more than 90% of the total oil content are indigestible wax esters (Alexander *et al.*, 2004; Ruiz-Gutierrez *et al.*, 1997; Yohannes *et al.*, 2002). Other lipid classes (hydrocarbon, triacylglycerol, sterol, and polar lipid) are present in small or negligible quantities. Moreover, both escolar and oilfish have high levels of histidine (8–11 mg/g) in their muscles (Feldman *et al.*, 2005; Kan *et al.*, 2000; Leask *et al.*, 2004).

A large and essentially unpredictable variability in the total oil and wax ester content of escolar was found with no clear correlation between the fish size and oil content. Also, no significant difference was found between the oil content of fish on the west coast and east coast of Australia, at least for specimens collected in summer (Ruello, 2004).

3. Effect of cooking on oil content and composition

Ruello & Associates Pty. Ltd. (Ruello, 2004) conducted a study for the Australian Government Department of Health and Ageing. A comparative study was made on baking and grilling escolar. Far more water than oil is lost during cooking as the total oil content on a wet-weight basis actually increases. Moreover, the cooking method has little effect on the oil composition; wax esters remain as the predominant oil class in the samples tested. The perception for the reduction of the volume or potency of the oil/wax ester in escolar by heavy grilling or other normal cooking method is unfounded. The notion of correct and incorrect cooking methods (with regards to keriorrhea) and that one cooking method is better than another (e.g., grilled vs. baked) is equally unfounded. Battering and frying are unlikely to raise the risk of keriorrhea. There was no evidence to support the common perception that wax esters can be ''grilled out'' of the fish or otherwise substantially reduced by normal cooking methods. Cooking actually ''concentrates'' the oil as water is expelled from the flesh. Freezing the (raw) fillet for as long as 9 months also failed to noticeably reduce the capacity of escolar to induce keriorrhea (Ruello, 2004).

B. Harmful effects

Escolar and oilfish have long been known to possess purgative effects because of their high oil content, accounting for approximately 20% of their wet weight (Cox and Reid, 1932; Gudger, 1925; Mori *et al.*, 1966c; Ukishima *et al.*, 1987). Substantial amounts of indigestible wax esters have been incriminated as the cause of keriorrhea and other acute gastrointestinal symptoms, such as abdominal cramps, nausea, headache, and vomiting in susceptible individuals (Alexander *et al.*, 2004; Ruiz-Gutierrez *et al.*, 1997; Yohannes *et al.*, 2002). Therefore, the wax esters in these two fish are regarded as a natural toxin called gempylotoxin (FDA, 2001a). Moreover, both escolar and oilfish have high levels of histidine in their muscles (Feldman *et al.*, 2005; Kan *et al.*, 2000; Leask *et al.*, 2004). If they are refrigerated improperly, bacteria can multiple and convert the histidine into histamine also termed scombrotoxin (FDA, 2001b), which can lead to cardiovascular, gastrointestinal, and neurological disorders (FDA, 2001b; Feldman *et al.*, 2005; Leask *et al.*, 2004).

C. Uses

Escolar and oilfish have been variously used as food. Oilfish has been traditionally used by Polynesians and Melanesians as a purgative medicine (Cox and Reid, 1932; Gudger, 1925). In the Union of the Comoros, an island nation in the Indian Ocean, oilfish is targeted as a food source and caught by local people regularly (Helfman *et al.*, 1999; Stobbs and Bruton, 1991). In Bermuda, oilfish is used as food and is acclaimed as an excellent eating (Gudger and Mowbray, 1927). In the Canary Islands and other seafaring regions in Spain, the fish is also used as a folk medicine in drinking broth made from the bones to relieve constipation (Raisfeld and Patronite, 2006; Ruiz-Gutierrez *et al.*, 1997). About 10 tons of escolar and oilfish were sun-dried and consumed annually in Japan before their sale was prohibited (Mori *et al.*, 1966c). Although described by health authorities as a purgative in Taiwan, they are openly sold and served as sashimi and fish steaks under the name You-yu (literally oilfish) (Fig. 1.3). Their roes (Fig. 1.4) are pressed and dried in Tungkang (Dunggang), Taiwan, and hailed as one of the three treasures of that little port as a new delicacy (Li, 2007). Compliments to the fish have come from many gastronomes. Berman *et al.*, (1981) commended that escolar had a very agreeable flavor with a soft, butter-like texture. Some people regard the fish as a delicacy; for instance, Bykov (1983) remarked in his book that ''The taste qualities of this fish (oilfish) are high. It is an excellent table fish.'' Raisfeld and Patronite (2006) praised it (escolar) as a dream fish, like toro (tuna), but cheaper.

FIGURE 1.3 You-yu sold as skinless and boneless fillet at fish market in Tungkang, Taiwan. The sample was identified as escolar using DNA sequencing by the authors (photo provided by authors).

The two fish are banned in Italy, Japan, and the Republic of Korea. In the rest of the world, they are generally not regarded as suitable for catering. As a result, they are frequently marketed and labeled as other more expensive commercial fish but at lower prices.

There are various suggestions for their exploitation, with the hope that their unusually high levels of wax esters could be utilized for the good of mankind. Wax esters derived from orange roughy and oreo dories have been included in various industrial processes like cleaning and degreasing (Nichols *et al.*, 2001). Wax esters enriched in ω3 LC-PUFA can be absorbed by rats, and wax esters are less prone to oxidation and can be better formulated than liquid ω3 derivatives (Gorreta *et al.*, 2002). Thus, wax esters enriched in ω3 can be a food supplement as there is increasing evidence that a diet high in ω3 LC-PUFA may help prevent coronary heart diseases (Iacono and Dougherty, 1993), and high level of wax esters in escolar and oilfish can act as a potential source for this purpose. Wax esters from escolar were processed by deacidification, decolorization,

FIGURE 1.4 You-yu roe retailed in Tungkang, Taiwan. One of the samples was identified as escolar using DNA sequencing by the authors (photo provided by authors).

hydrogenation, and distillation to obtain a semisolid wax at room temperature; the refined wax was tested safe and useful as a base for medicine and cosmetics (Ukishima *et al.*, 1987). A further value-added process involved removal of most of the lipid from escolar meat by repeated alkaline washing to make a gel, which was tested and found to be a better raw material than the commercial bigeye snapper used currently for surimi (ground fish meat) production (Pattaravivat *et al.*, 2008).

Additionally, on the internet, there are discussions on the possibility of using escolar and oilfish for slimming or weight reduction. The value of this application is doubtful as only the oil (wax esters) would be discharged.

D. Supply

As escolar and oilfish are widely distributed in the tropical and temperate seas, they are frequently caught and marketed as a result of by-catch with other commercially important species (Mori *et al.*, 1966c; Tserpes *et al.*, 2006). It was reported that about ten tons of by-catch oilfish and escolar were sun-dried and consumed annually in Japan before the sale prohibition was implemented (Mori *et al.*, 1966c). Up to 400 tons of escolar are caught annually in Australia (Shadbolt *et al.*, 2002). In 2003, escolar catch accounted for up to 16,501 tons of total by-catch species in longline fishing conducted by the Southern and Western Tuna and Billfish Fishery

(Lynch, 2004). In a report on the by-catch of tuna longliners from a South Korean observer program, escolar and oilfish ranked the second (20.8%) and third (15.6%) most common by-catch fish species, respectively (Yang *et al.*, 2005). According to the US National Marine Fisheries Services, annual landings of escolar varied between 40 and 80 tons from 1999 to 2007, while that of oilfish increased from 32.4 tons in 1999 to 216.3 tons in 2007 (Figs. 1.5A and B) (NMFS, 2008). Taiwan has a decade-long record of oilfish harvest, and the annual catch increased 15-fold from 2,700 tons in 1999 to near 42,000 tons in 2007 (Fig. 1.6).

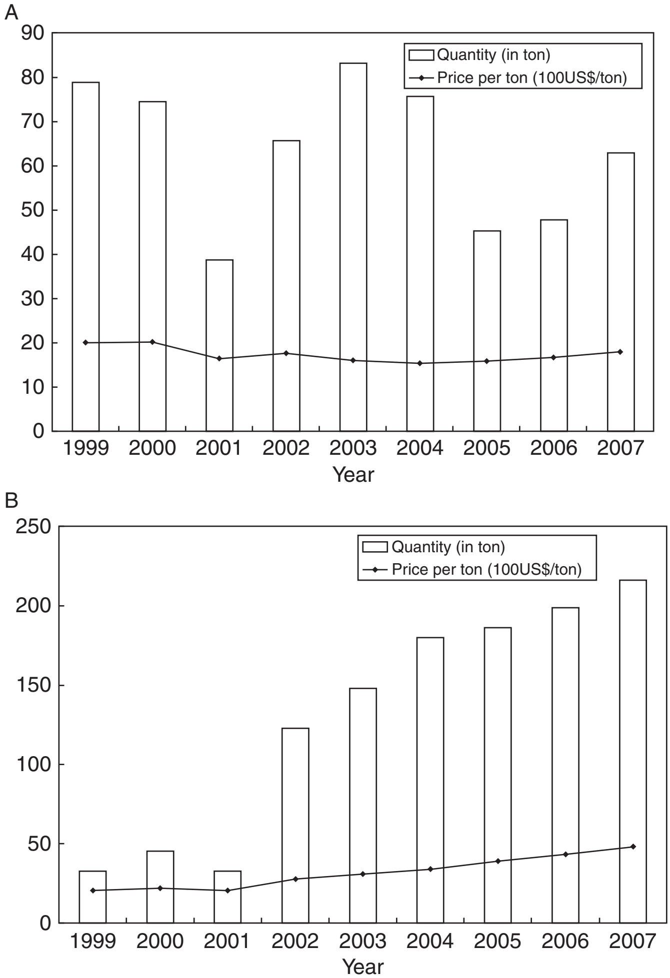

FIGURE 1.5 (A) The landing quantity and price of escolar in the US from 1999 to 2007. (B) The landing quantity and price of oilfish in the US from 1999 to 2007. Data from NMFS (2008), National Marine Marine Fisheries Services Annual Landings Database.

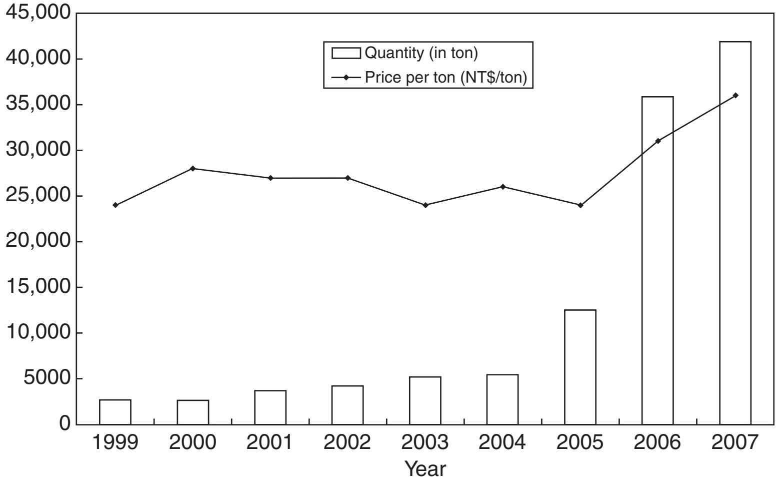

FIGURE 1.6 The landing quantity and price of oilfish in Taiwan from 1999 to 2007. Data from Taiwan Fisheries Agency (1999–2007, Taiwan Fisheries Yearbook).

In the market, escolar is often deep skinned, and the skin and red muscle are discarded. The longitudinal portion of muscle tissues is cut parallel to the backbone and then into chunks or blocks of white skinless and boneless fillets. In sushi bars or fish markets, escolar chunks are cut into slices and served as sashimi in Hong Kong and Taiwan under the names of Bai-yu-tuan and You-yu, respectively. Escolar of smaller sizes may be cut into transverse sections through the backbone, and the cutlets are retailed with the skin on (Ruello, 2004). Oilfish, on the other hand, is more often retailed as cutlets. The scales on the outside of the fish are removed, leaving big grayish quadrangular patterns of the skin remaining on the cutlets.

E. Mislabeling and mishandling

Escolar and oilfish are of low commercial values because of their kerrior-rheic properties. They are considered as ''not suitable for catering'' or even banned from sale in various countries. However, they are commonly marketed as a result of their substantial by-catch with tuna and swordfish (Shadbolt *et. al.*, 2002; Tserpes *et al.*, 2006). According to the European Communities (Labelling of Fishery and Aquaculture Products) Regulations 2003 (S.I. No. 320 of 2003), *L. flavobrunneum* and *R. pretiosus* must be marketed as escolar and oilfish, respectively, and no other commercial names can be used alternatively. Yet, both species are usually mislabeled as sea bass, butterfish, rudderfish, white tuna, or codfish either intentionally or accidentally. Under these circumstances, outbreaks of keriorrhea associated with consumption of escolar or oilfish have been repeatedly reported in several continents (Berman *et al.*, 1981; Feldman *et al.*, 2005; Givney, 2002; Gregory, 2002; Jacquet and Pauly, 2008; Leask *et al.*, 2004; Ling *et al.*, 2008a,b; Shadbolt *et al.*, 2002; Waldman *et al.*, 2006).

Besides wax ester poisoning, escolar and oilfish are common candidates for histamine poisoning, which has a greater affect than keriorrhea and can cause more serious manifestations. Escolar and oilfish contain high levels of histidine in their muscles (Feldman *et al.*, 2005; Kan *et al.*, 2000; Leask *et al.*, 2004). If these fish are inadequately refrigerated, bacteria can multiply and convert histidine into histamine, also termed scombrotoxin (FDA, 2001b). This conversion often happens when large numbers of unsold fish steaks are stocked over time to avoid food inspection in case of a related keriorrhea outbreak. The fish may reappear later in markets, but at that time, the steaks may be contaminated and not suitable for consumption. Scombrotoxin, like wax esters, is heat stable and is not destroyed by cooking; it can lead to cardiovascular, gastrointestinal, and neurological disorders (FDA, 2001b; Feldman *et al.*, 2005; Leask *et al.*, 2004). Therefore, detection of wax esters could help prevent more severe food poisoning from happening once any keriorrhea outbreak is reported (Ling *et al.*, 2008a,b).

F. Global concerns

Australia, Canada, the United States, and a majority of member states of the European Union have issued special guidelines toward trading and consumption of the two fish. Italy and Japan have banned their import and sale (Alexander *et al.*, 2004) before 2007. However, outbreaks of keriorrhea are still reported occasionally across continents. Recently, an outbreak of over 600 cases of keriorrhea occurred in Hong Kong toward the end of 2006 (Chong, 2007; Chung, 2007a; Connolly *et al.* 2007; Jacquet and Pauly, 2008; Ling *et al.*, 2008a,b). The packages of oilfish cutlets were mislabeled as codfish (Chong, 2007; Ling *et al.*, 2008a,b). Escolar, on the other hand, was found offered as sushi or sashimi under the name of snowfish or white tuna (Chung, 2007b; Ling *et al.*, 2008a,b; Mok, 2007). In February 2007, similar fish cutlets were found in Chinatown in Toronto, Canada, and resulted in a keriorrhea mini-epidemic there. Three months later (May 2007), the oily fish was found sold as white tuna sushi in South Korea and several cases of illness were reported, leading to the South Korean government prohibiting the use of oilfish and escolar for human food and banning any import of the fish in August 2007 (Stenhouse, 2007). Escolar- or oilfish-related illness has long been recognized, yet the problems have never been eradicated and still occur repeatedly (Shadbolt *et al.*, 2002). The public always express great concern over this problem; for instance, the oilfish scandal in 2006 awoke the Hong Kong public to this food safety issue and there were strong demands for regulating and identifying these two fish (Goh, 2007). Indeed, voices to completely ban the fish are on the rise. The industry, however, holds an opposite opinion and insists that the two fish are not toxic and are suitable for catering provided that certain guidelines are followed. In addition, there are great individual differences in terms of susceptibility. Some people consider the fish as a delicacy and enjoy the fish without problems, while others experience frequent keriorrhea (Ruello, 2004). Therefore, it is a dilemma for the responsible agencies as to whether to ban the two fish. As a result, different countries have different rules and the rules also change with time making it a nightmare to food safety and control agencies in case of further outbreaks.

III. REGULATION AND LITIGATION

A. Regulation

Because of the differential impact of escolar- or oilfish-related problems around the world, and also variation in individual susceptibility, different governments continue to promulgate only modest regulation on both fish. Only three countries, Japan, South Korea, and Italy, completely ban the trading and import of the two fish, while other countries only issue special guidelines or warnings toward them (Table 1.2). It therefore remains that the majority of countries do not have any regulations for the two fish.

B. Litigation

Although outbreaks of keriorrhea have repeatedly occurred worldwide, it is rare to find cases of prosecution or litigation. However, recently in Hong Kong, a supermarket chain was fined over selling oilfish mislabeled as codfish (Lau, 2007; Wong and Lam, 2007). In that case, a total of 14 complaints were received by the Hong Kong Centre for Food Safety regarding diarrhea or serious stomach upsets after consumption of fish cutlets labeled as cod purchased from the supermarket chain. It was later confirmed that the so-called cod fish was actually oilfish. The Food and Environmental Hygiene Department, HKSAR, later initiated prosecution toward the supermarket chain. Finally, the supermarket chain pleaded guilty of selling food not of the substance expected by consumers and was fined HK$45,000 for mislabeling oilfish as cod and ordered to pay the cost of laboratory tests. In Hong Kong, sale of oilfish is not regulated because it is not considered poisonous. The magistrate, however, still condemned

TABLE 1.2 Polices on escolar and oilfish in various countries or cities

Country/city	Authority	Action/recommendation	References
Australia	Queensland Health, Queensland Government	No ban. Recommended that the fish are not suitable for catering	Queensland Health (2008)
Canada	Canadian Food Inspection Agency	No ban. Recommended to choose smaller portion sizes and prepare the fish in a way to reduce oil content	CFIA (2007)
Denmark	Danish National Food Administration	No ban. Cautioned the Danish fish importing companies and issued cooking and storage recommendations	Alexander *et al.* (2004)
European Union member states	European Food Safety Authority, European Union	No ban. Issued opinion from advisory group. Recommended a notification to public of the potential health risks and proper preparation practices	Alexander *et al.* (2004)
German	German federal Institute for Risk Assessment	No ban. Published information concerning potential problems in connection with the consumption of the fish	Alexander *et al.* (2004)
Hong Kong	Centre for Food Safety	No ban. Issued guidelines on labeling and handling the fish	WGNCO (2007)

Italy	N/A	Banned import and sale	Alexander *et al.* (2004)
Japan	Japanese Ministry of Health and Welfare	Banned import and sale	Kawai *et al.* (1985)
Macau	Department of Health	No ban. Recommended the fish are not suitable for catering	Macau Disease Control Centre (2007)
Singapore	Agri-Food and Veterinary Authority	No ban. Issued notification of the potential health risks and required proper labels	Chua (2007)
Sweden	Swedish National Food Administration	No ban. Cautioned the Swedish National Fish Trade Association and issued cooking and storage recommendations	Alexander *et al.* (2004)
United Kingdom	Food Standards Agency	No ban. Issued notification of the potential health risks and mislabeling problems of the fish	Statham (2003)
USA	Food and Drug Administration	Reversed to no ban. Advised against the sale of the fish in intrastate/interstate commerce, and requested warning labels	Yohannes *et al.* (2002)

the supermarket chain for contravening food safety regulation (Public Health and Municipal Services Ordinance, Hong Kong Laws Chapter 132) by failing to ensure its products were safe and labeling accurate, and pointed out that the supermarket had committed very serious offence in selling, without warning, a product that was generally unsuitable for human consumption.

IV. BIOCHEMISTRY AND TOXICITY

A. Wax esters and their biological roles

Wax esters are carboxylic esters consisting of a fatty acid esterified to a fatty alcohol (Fig. 1.7), wherein both the acids and alcohols can be either saturated or unsaturated (Kolattukudy, 1976). Wax esters are present in different organisms, from the seeds of jojoba to the head oil of sperm whale (Busson-Breysse *et al.*, 1994; Spencer *et al.*, 1977; Takagi *et al.*, 1976). Wax esters serve a variety of biological functions; for instance, they are used as energy reserve in seeds and roes, provide buoyancy in dinoflagellates and pelagic invertebrates, and prevent water loss as in the waxy layer on the cuticle of insects (Joh *et al.*, 1995; Nelson *et al.*, 2000; Phleger, 1998). Although wax esters can be found across different taxa, the major muscle lipid components of most fish species, including many commercially important fish, are triacylglycerols and phospholipids. Wax esters, in contrast, are considered less common lipid components, and where they occur in deep-sea fish species provide a way to enhance buoyancy (Bone, 1972; Lee and Patton, 1989). The source of such a high level of wax esters (up to 20% of wet weight) in escolar and oilfish is still unknown, but may possibly be formed by similar mechanisms as in another wax ester-rich fish, orange roughy (*Hoplostethus atlanticus* Collett). The ability to synthesize large amounts of long-chain alcohols is the key to determine whether a marine animal produces wax ester or triacylglycerols as its major neutral body lipid (Lee and Patton, 1989). In a study of wax esters synthesis in *Euchaeta norvegica*, which is a wax ester-rich zooplankton, radio-labeled glucose or alanine was given to the organism and most of the radioactivity in the wax esters was detected in the alcohol moiety, implying that fatty alcohols are synthesized *de novo* from nonlipid precursors, while the fatty acids in wax esters are sourced from dietary fatty

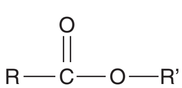

FIGURE 1.7 The basic structure of a wax ester (R = fatty acid chain; R′ = fatty alcohol chain).

acids (Henderson and Sargent, 1980). Sargent *et al.* (1983) in their study of orange roughy suggested that the wax esters could be produced by (a) *de novo* biosynthesis of 20:1 and 22:1 fatty acids that are then reduced to fatty alcohols, (b) chain elongation and desaturation of shorter chain dietary fatty alcohols and fatty acids to yield long chain fatty acids that are finally reduced to alcohols, or (c) or modification of dietary fatty alcohols and acids. In orange roughy, wax esters are stored extracellularly (Phleger and Grigor, 1990). Extracellular wax esters serve only for buoyancy. The storage of wax esters could be superior to that of triacylglycerols under certain physiological situations. A unit volume of wax esters provide approximately 70% more upthrust than the same volume of triacylglycerols in seawater with a density of 1.025 g/cm^3 (Sargent, 1978). In addition, wax esters are essentially noncompressible, and are superior to a gas-filled swim bladder, during vertical migration (Phleger *et al.*, 1999). Escolar and oilfish, which both lack a swim bladder, could travel vertically at depths between 100–800 m and 200–1100 m, respectively (Nakamura and Parin, 1993), and wax esters provide them with better buoyancy control. High concentrations of wax esters in the fish skin, like the function of wax ester-rich blubber in whale, help insulate them from the freezing deep-sea environment. Indeed, oilfish, similar to orange roughy, has the highest oil content (32.3%) in the integument (Bone, 1972).

B. Toxicity

It was reported that most people experience keriorrhea without bowel cramps or abdominal discomfort, implying that the frequent passage of oil in most people is caused by the lubricant effect of the oil, but not by an irritant effect as in the case of toxic substances in ordinary diarrhea (Du Plessis *et al.*, 2004). Oilfish was previously called ''castor-oil fish'' based on an erroneous report that its oil was composed of 13% hydroxyoleic acid (Gudger, 1925) and a mistaken test that falsely indicated a similar purgative ability between the fish oil and castor oil (Cox and Reid, 1932). Unlike wax esters, hydroxyoleic acid, which is the purgative chemical in castor oil, causes diarrhea by an irritant effect on the bowel instead of the lubricating and pooling effects of wax esters to the rectum (Berman *et al.*, 1981). Indeed, studies revealed that hydroxyoleic acid is unlikely to be present in oilfish (Mori *et al.*, 1966c; Nevenzel *et al.*, 1965). Wax esters are not destroyed or decomposed during cooking. Resistance to digestive enzymes, such as lipase, and a low melting point (in oily state at human body temperature) results in pooling of large amount of these lubricant wax esters in the rectum leading to keriorrhea.

In a strict sense, wax esters are not completely indigestible in mammals. Wax esters are hydrolyzed by lipases at a very slow rate and the products, especially fatty alcohols are only slowly absorbed. Therefore, dietary wax esters are little absorbed and the majority is excreted in a mixture of wax esters (altered or unaltered) and fatty alcohols. Rats that were fed with single small doses of cetyl palmitate (major wax ester in spermaceti) had triacylglycerols present in the lymph (Munk and Rosenstein, 1891). Large doses of mutton-bird oil (mainly as cetyl and oleyl oleates) fed to rats were partially absorbed (Carter and Malcolm, 1927). It was also true for cats that cetyl esters and cetyl alcohols were found in the feces (Carter and Malcolm, 1927). Moreover, rats on a diet with 15% jojoba oil (rich in wax esters) absorbed 70% and excreted the remainder as wax esters and free alcohols, while a purgative effect was observed for this type of diet (Savage, 1951). Again, partly absorbed and partly excreted wax esters and free alcohols were observed in rats fed with feeds containing 15% of oleyl palmitate (Hansen and Mead, 1965).

There is no specific wax ester digestive lipase in mammals. Hydrolysis of wax esters is carried out by the same lipase that also acts on triacylglycerols. Savary (1971) showed that purified mammalian pancreatic lipase is 10–50 times slower in hydrolyzing wax esters than triacylglycerols. The reasons for a much slower hydrolysis of wax esters by lipase are product inhibition and hydrophobicity. The hydrolyzed products, fatty alcohols and fatty acids, form an oil or solid phase in water. The products diffused only slowly out of the oil-water interface and the bulk of insoluble reaction mixture cause ''product smothering'' to the water-requiring lipase (Lee and Patton, 1989). Moreover, the large amount of slowly absorbed, thus accumulated, fatty alcohols could reverse the reaction and result in synthesis of wax esters. Hansen and Mead (1965) showed that synthesis of waxes can occur in the intestine of rats fed with oleyl alcohol (fatty alcohol). The hydrophobic nature of wax ester molecules can hamper their interaction with the active site of lipase (Lee and Patton, 1989). All of these properties engender a very ineffective hydrolysis of wax esters, and if a large dose of wax esters is consumed, much of the wax esters are passed through the intestines without digestion and absorption. Therefore, a pooling of large amounts of these lubricant wax esters in the rectum leads to keriorrhea.

Data from one escolar-associated outbreak found no correlation between BMI, age, health status, and amount of fish consumed to the severity and occurrence of symptoms, while other factors, such as variability in wax ester content in different fillet cut depths, could be relevant (Yohannes *et al.*, 2002). Unlike some fish species, such as herring, which have uniform muscle oil content along the body (Brandes and Dietrich, 1953), muscle oil content in escolar and oilfish is not evenly distributed. Bone (1972) found that muscle oil content in oilfish increases from 14.5% (near vertebral column) to 24.7% (near the skin). A similar trend was also observed by Ruiz-Gutierrez *et al.* (1997) with higher oil content found in subcutaneous muscles than the periosteum. However, the lipid profile for dorsal and ventral muscle portions is much the same (Ruiz-Gutierrez *et al.*, 1997). Moreover, there is a tendency that muscle oil content is higher at the anterior part and decreases toward the posterior end (Bone, 1972). The highest oil content (32.3%) is found in the integument (Bone, 1972). Wax ester content in a fish species also could vary with environmental factors, such as catch location, diet of the fish and physiological factors, such as gender and reproductive stage (Nichols *et al.*, 2001). For instance, wax ester content in mullet increased sharply in the roes during the reproductive season (Iyengar and Schlenk, 1967). Seasonal variation of wax ester content may account for the fact that a majority cases of oilfish-related outbreaks in Australia occurred between August and November (Doyle, 2002).

Although painless, keriorrhea was frequently reported as the only symptom associated with escolar consumption (Berman *et al.*, 1981; Ruello, 2004). Other reports, however, recorded much severer symptoms, such as abdominal cramps, nausea, headache, and vomiting, after escolar consumption (Yohannes *et al.*, 2002). Yohannes *et al.* (2002) indicated that scombroid (histamine) poisoning was unlikely the reason for the severer symptoms in the 2002 outbreak, given that the onset was very rapid (45 min) while symptoms common for scombroid poisoning, including fever, flushing, and rapid pulse rate, were not detected.

C. Animal tests

A limited number of studies have been performed with animals. In one case, two cats were fed 20 g of escolar flesh each. The smaller cat weighing 530 g exhibited diarrhea with frequent watery stools 4 h after consumption, while the larger animal weighing 810 g did not show any diarrhea (Mori *et al.*, 1966c). Due to the limited sampling size and the experimental design, the divergent responses could be due to a difference in sensitivity or dosage level; the smaller cat consumed approximately 50% more flesh (0.038 g flesh/g body weight) than the larger one (0.025 g flesh/g body weight) in terms of the flesh consumed per unit body weight.

Toxicity of the wax esters from escolar and oilfish was also assessed in rats (Mori *et al.*, 1966c). A total of 20 rats were divided into five groups. The test groups were fed daily with rice, casein, yeast, and salt mixture together with escolar flesh (7.5 g), oilfish flesh (7.5 g), escolar oil (1.5 g), or oilfish oil (1.5 g), while the control group was fed the same without the flesh or fish oil. Signs of seborrhea, with oil smudging on hairs, mouth, and belly, was observed on the second day of feeding in all, except the control, groups. All 16 rats fed with either flesh or fish oil showed diarrhea and 13 of them died within 10 days.

Seborrhea is another long-term side effect of eating the oily fish. Wax esters are released through the sebaceous gland of the skin, blocking the pores and potentially interfering with metabolism. Seborrhea and acute fatality was reported in animals fed with various wax esters (Matsuo, 1962), but not by Hansen and Mead (1965), where rats were fed with oleyl palmitate.

Two studies conducted on orange roughy, another deep-sea fish rich in wax esters, can be illuminating. Rats were fed for 28 days a diet containing various amounts of flesh from orange roughy. Rats on a low dose diet of less than 360 g orange roughy/kg body weight (~30 g wax esters/kg body weight) displayed no observable difference from the control groups on a wax ester-free diet. In the group fed with 540 g orange roughy/kg (~44 g wax esters/kg), persistent oiliness around the anus and fecal smudges on food pots were observed. The hairs over the whole body became heavily coated with oil and the excretion of oily feces was observed in the groups on a diet of 720 and 1430 g orange roughy/kg. All rats on 2870 g orange roughy/kg (~233 g wax esters/kg) diet died within 11 days (James and Treloar, 1984). The second study was on pigs fed with orange roughy flesh at 6.7 g/kg/day (equivalent to a daily fish meal of 500 g for an average person of 75 kg body-weight) over an extended period (starting from live weight at 20 kg until 80 kg). All pigs stayed healthy and gained weight throughout the whole period. No purgative effect was observed (James and Body, 1986). Based on these results, the two reports concluded that normal consumption of small portions of orange roughy by humans generally would not cause any serious health problem. An estimate of the safety window can also be made by taking into consideration the fact that escolar and oilfish have three to four times more wax esters than orange roughy (Nichols *et al.*, 2001).

D. Human studies

No clinical studies are available, except three reports that described volunteer tests on the responses after consumption of escolar or oilfish (Berman, *et al.*, 1981; Cox and Reid, 1932; Ruello, 2004). In the study by Cox and Reid (1932), one of the authors ingested an ounce (about 28 g) of extracted oilfish oil (equivalent to about 140 g of oilfish flesh) and reported no symptoms. In the second study (Berman *et al.*, 1981), two of the authors consumed about 500 g of baked escolar flesh. They found the fish to have a very agreeable flavor with a soft, butter-like texture. After 12 symptom-free hours, oil began to be passed *per rectum*. It was difficult to contain the oil that was pooling in substantial quantities in the lower rectum, and therefore frequent evacuation was necessary. Approximately 10 ml of oil were passed on one occasion. The oil was clear orange or green in color, inoffensive in odor, and not on most occasions contaminated significantly by fecal material. The authors did not experience any bowel cramps or visceral discomfort, suggesting that the discharges were caused by the lubricant effect of the oil, rather than by any irritant action. The oil passed *per rectum* was further analyzed and confirmed as wax esters, suggesting that wax esters were not digested in humans and passed through the gastrointestinal tract unchanged.

In the third report (Ruello, 2004), the author and his wife consumed 140–260 g of baked or grilled escolar flesh on seven occasions with remarkably different experiences and varying degrees of painless keriorrhea. The author experienced a very mild to heavy form of keriorrhea after each meal of fresh or frozen fish, while his wife experienced only one episode of mild keriorrhea. According to the author, it was typical keriorrhea and painless passage of oil *per rectum*, with no diarrhea (watery liquid feces) at any stage. He also highlighted the potential for embarrassment from stained clothing arising from the unanticipated passage of oil as an aerosol with flatulence (or when at the toilet). Although the limited and informal records may not be conclusive, the author did emphasize that the one larger portion of 260 g did lead to ''an unsettled lower intestine'' and discomfort at 6 h after consumption and stronger oil flow, whereas the smaller portions triggered milder keriorrhea with an onset time at 13 h post ingestion. The author also added that, in a casual trial by nine informed volunteers on 150–180 g of escolar fillet, only three reported mild doses of orange oil discharge for about two days after the meal.

Based on the three volunteer trial reports and the summaries of outbreak episodes, it may be concluded that typical keriorrhea resulting from consumption of reasonable portions of escolar or oilfish fillet will lead to oily discharges generally without warning 1–36 h after ingestion. Frequent urges for bowel movements occur due to the lubricant qualities of the indigestible wax esters accumulated in the rectum. These symptoms are generally not accompanied by other discomfort nor diarrhea. Such responses after intake of escolar or oilfish flesh are not obligatory and vary among people due to individual sensitivity. There is a possibility that other symptoms such as stomach cramps, loose bowel movements, diarrhea, headache, nausea, and vomiting, as reported in various outbreaks, are incidental or due to embarrassment, anxiety, and panic induced by keriorrhea. It is also likely that diarrhea is a wrong descriptive used by confused victims suffering from keriorrhea.

V. IDENTIFICATION AND DETECTION

A. Morphological and anatomical analyses

Oilfish is usually sold as cutlets with integument and bone still attached (Fig. 1.8). Bone (1972) studied the musculature of oilfish and found that it possesses a high proportion of white muscle (80%) and little red muscle in

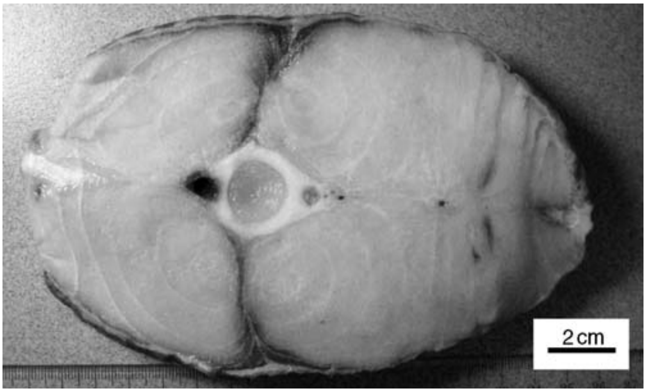

FIGURE 1.8 Oilfish cutlet. (photo provided by authors).

FIGURE 1.9 Oilfish fillet. (Regulatory Fish Encyclopedia, U.S. FDA, 1993–2008, reprinted with permission).

the myotomes (Figs. 1.8 and 1.9). Oil stored in bone is not infrequent in fish, but the high oil content in oilfish skeletal elements (21.1% in vertebral bone and 30.5% in frontal bone) is remarkable (Bone, 1972). The bone structure is indeed a girder system enclosing oil sacs, making the bone significantly less dense than water (Bone, 1972). Consumers are advised not to suck the bones because of the notably high oil content (Nordhoff, 1928). The integument of oilfish is covered with characteristic ctenoid scales with scattered pores of various sizes (Fig. 1.10) (Bone, 1972). The pores are connected to a large system of subdermal space, which can be observed in the transverse section of the fish (Bone, 1972). The characteristic integument of oilfish, if not removed, can assist a trained eye to

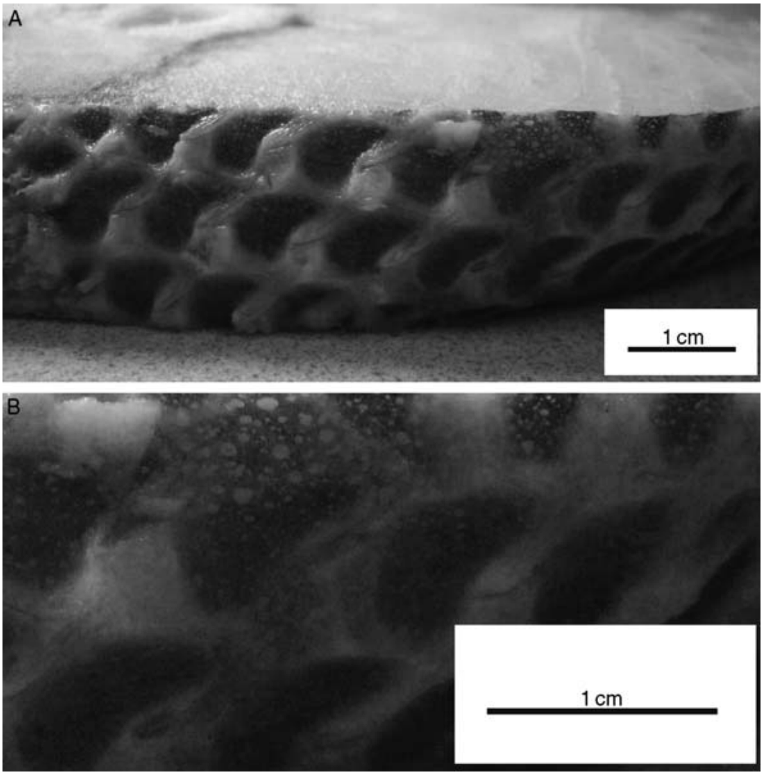

FIGURE 1.10 (A) Oilfish integument; (B) close up of oilfish integument (photos provided by authors).

identify the fish. In contrast, escolar is often sold as fillets without skin (Fig. 1.11), making it difficult to reach a definitive identification. When the whole fish is available, the highly undulating lateral line in escolar is a distinguishing characteristic (Figs. 1.2B and 1.12), which was used for identification purposes in an outbreak of histamine poisoning (Kan *et al.*, 2000). An additional characteristic for the two fish is that they are exceptionally oily to the touch.

B. Protein analysis

Polyacrylamide gel electrophoresis (PAGE) and cellulose acetate membrane electrophoresis (CAME) were applied to distinguish escolar and oilfish from 27 commercial fish based on muscle protein differences (Ochiai *et al.*, 1984). Myogen fractions from the muscles were subjected

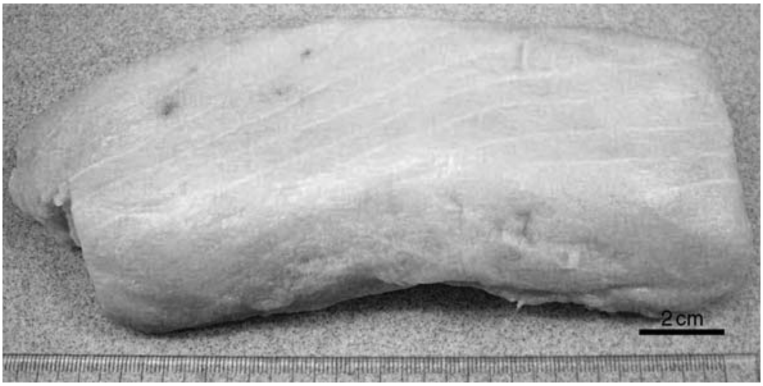

FIGURE 1.11 Escolar sashimi purchased in Japanese restaurant in Hong Kong (photo provided by authors).

FIGURE 1.12 Fillet from escolar (Regulatory Fish Encyclopedia, U.S. FDA, 1993–2008, reprinted with permission).

to either PAGE with Coomassie brilliant blue staining or CAME with Ponceau 3R staining to visualize the protein profile. The gel was also stained for lactate dehydrogenase (LDH) and malate dehydrogenase (MDH) activities to look for characteristic patterns to identify escolar and oilfish. Ochiai *et al.* (1984) concluded that the myogen protein could be used to distinguish escolar and oilfish from other fish, while both dehydrogenase (LDH and MDH) did not give species-specific pattern. Moreover, PAGE is said to be better than CAME for the purpose. However, if fish is processed by cooking or sun-drying, the species-specific proteins could be denatured (Carrera *et al.*, 1999).

C. DNA analysis

In contrast to the heat-labile proteins, DNA is relatively stable and can be tested in samples heated up to 120 °C (Lenstra, 2003). It is, unlike proteins, less affected by physiological conditions, environmental factors, storage, and processing (Shaw *et al.*, 2002). DNA sequences are now widely used for species identification in DNA barcoding (Ratnasingham and Hebert, 2007). Species identification can be made by sequence searches on public sequence databases, such as GenBank (www.ncbi.nlm.nih.gov) and BOLD (www.barcodinglife.org). DNA sequencing, which determines the actual nucleotide types and arrangements in amplified DNA fragments, is used to differentiate escolar and oilfish from other commonly marketed fish (Ling *et al.*, 2008a,b). Four mitochondrial DNA regions, namely 12S rRNA gene, 16S rRNA gene, cytochrome b gene, and cytochrome oxidase subunit I (COI) gene, were sequenced and the results confirmed that some codfish samples on the market were actually oilfish. The four regions were used to construct four neighbor-joining (NJ) trees and they were all useful in distinguishing escolar and oilfish and differentiating the two fish from other fish (Fig. 1.13). DNA sequencing was also successful when applied to cooked oilfish samples.

D. Lipid analysis

Escolar and oilfish contain a mixture of wax esters with different carbon-chain length, mainly C32, C34, C36, and C38, formed by combining different fatty acids and fatty alcohols. The dominant fatty acids in escolar and oilfish wax esters are the monounsaturated fatty acids (Table 1.3), namely oleic acid (18:1ω9) and eicosenoic acid (20:1ω9), while the dominant fatty alcohols are saturated and monoenoic fatty alcohols (Table 1.4), known as cetyl alcohol (16:0) and oleyl alcohol (18:1ω9). PUFA, which are trace components in muscle wax esters, are commonly found in wax esters from roe, they include 20:4ω6, 20:5ω3, 22:5ω3 and 22:6ω3. These differences could be due to the functional role in muscle for providing buoyancy, while that of roe is to store energy and key essential PUFA for fry development (Lee and Patton, 1989).

Wax esters are more hydrophobic than analogous triacylglycerols. For each hydrocarbon chain in triacylglycerols there is one hydrophilic ester group, whereas in wax esters there is one-half of an ester group (Lee and Patton, 1989). Thus, long-chain wax esters are classified as nonpolar lipids with triacylglycerols being somewhat more polar. This small difference in polarity is applied to separate wax esters from triacylglycerols and other lipids using chromatography (Lee and Patton, 1989). The unusually high levels of wax esters in escolar and oilfish allow thin-layer chromatography (TLC) or gas chromatography to be applied to differentiate the

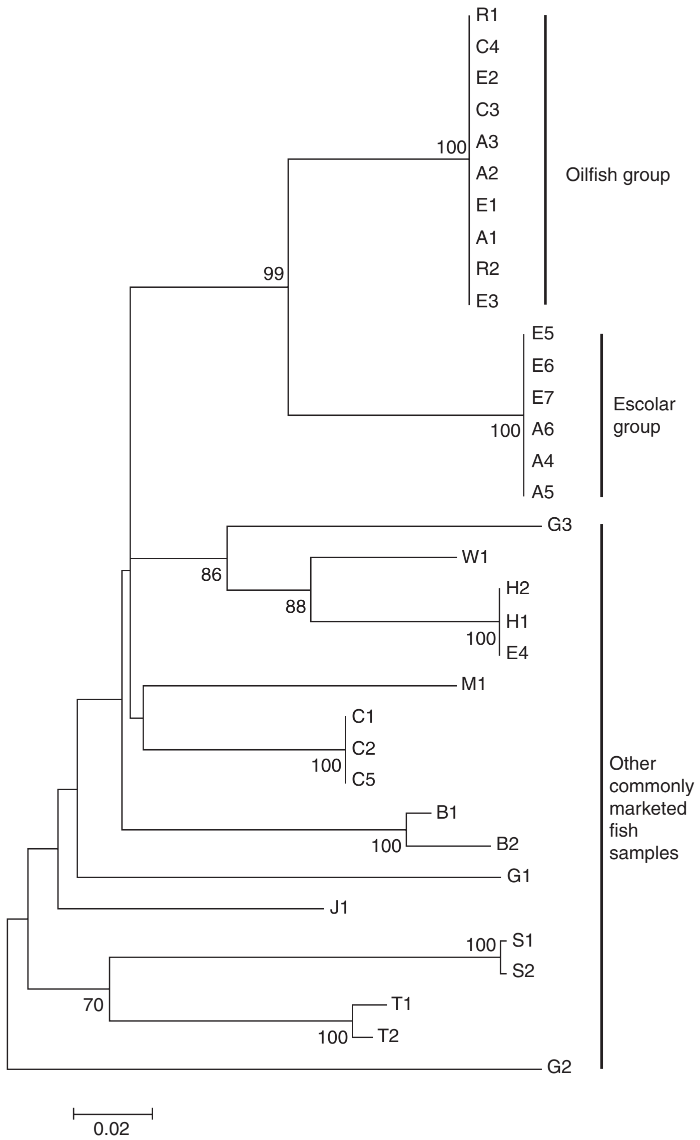

FIGURE 1.13 The neighbor-joining (NJ) trees for 12S rRNA gene sequences from 34 fish samples. Escolar and oilfish could be distinguished from other commonly marketed fish (including cod, sea bass, salmon, catfish, swordfish, halibut etc.) (Ling *et al.*, 2008a,b; data from authors).

two fish. Ling *et al.* (2008a,b) used TLC to rapidly differentiate escolar and oilfish from other wax ester-absent fish. In that study, lipid was extracted by hexane and applied to silica gel plates. The plate was developed in a

TABLE 1.3 The major fatty acids in the wax esters of escolar and oilfish muscle

	Fatty acids (R chain in Fig. 1.7)	Escolar (%) [a](a and b)	Oilfish (%) [a](a and c)
16:1	Palmitoleic acid	1.1/2	1.8/3.7
18:1	Oleic acid	64.2/80	72.1/47.7
20:1	Eicosenoic acid	24.7/15	10.9/6.9

[a] Data as in a: Mori *et al.* (1966c); b: Berman *et al.* (1981) and c: Ruiz-Gutierrez *et al.* (1997).

TABLE 1.4 The major fatty alcohols in the wax esters of escolar and oilfish muscle

	Fatty alcohols (R′ chain in Fig. 1.7)	Escolar (%) [a](a, b, and c)	Oilfish (%) [a](a)
14:0	Myristyl alcohol	3.1/3/2.6	2.5
16:0	Cetyl alcohol	33.7/43/52.6	48.1
16:1	Palmitoleyl alcohol	4.1/5/3.9	7.4
18:0	Stearyl alcohol	10.4/10/8.9	5.3
18:1	Oleyl alcohol	24.6/16/24.9	29.5
20:1	Eicosenol	11.2/15/2.7	1.5

[a] Data as in a: Mori *et al.* (1966c); b: Berman *et al.,* (1981); and c: Nichols *et al.,* (2001).

glass tank lined with filter paper and saturated with xylene, which was the mobile phase for resolving nonpolar lipids. After development, the plate was oven-dried and sprayed with 40% sulfuric acid in ethanol: anisaldehyde (9:0.1), and heated at 100 °C until color was observed. A characteristic spot at Rf = 0.6, which belongs to the nonpolar wax esters, was found only in escolar and oilfish (Fig. 1.14). Because wax esters are heat-stable, cooked oilfish samples showed an identical TLC spot to the untreated oilfish samples. Nichols *et al.* (2001) analyzed the nonsaponifiable lipids of escolar and oilfish by gas chromatography and TLC-flame ionization detection and revealed that the lipid class profiles and the wax ester-derived fatty alcohol profiles readily distinguish the two fish from other wax ester-rich fish, such as orange roughy and six species of deep-sea oreos. The lipid class and fatty alcohol profiles of escolar and oilfish are very similar, although oilfish has higher levels of 18:1ω9 and 16:1ω7, and lower levels of 18:0 than escolar (Nichols *et al.*, 2001). Based on the subtle differences in lipid class and fatty alcohols profiles, two unknown fillet samples associated with an outbreak of keriorrhea was traced to escolar (Nichols *et al.*, 2001).

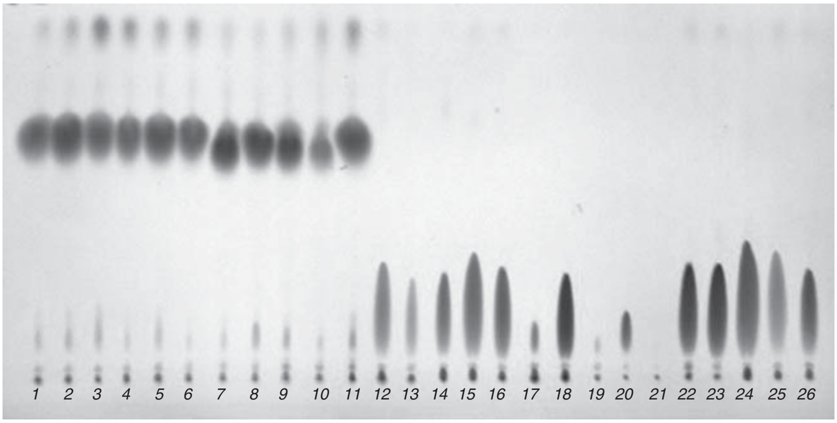

FIGURE 1.14 Thin layer chromatogram of oil extracted from 26 fish samples observed under visible light. Only oilfish (lanes 1–7, 11) and escolar samples (lanes 8–10) showed a characteristic spot at Rf = 0.6 (Ling *et al.*, 2008a,b; data from authors).

VI. WAX ESTER-RICH FISH AND OTHER POTENTIAL HAZARDS

A. Gempylidae family

Escolar and oilfish are the only species of their respective genera (Alexander *et al.*, 2004; Nakamura and Parin, 1993), and there are another 22 species in the same family, Gempylidae (Table 1.5). Species in this family share similar characteristics and thus these species may contain indigestible wax esters in their muscle. There is evidence that the presence of wax esters is an environment-based characteristic rather than a phylogeny-based character; for example, the deeper-living members in Mycophidae have higher wax ester contents than the epipelagic species of the same family (Nevenzel *et al.*, 1969). However, examination of the lipid content and composition in other species of the Gempylidae family, except escolar and oilfish, is limited, and further investigation appears warranted to both inform industry, health authorities, and government agencies and also to safeguard the public.

B. Other deep-sea fish

Fish with more than 10% wax esters in the total lipids of body tissues are uncommon. When higher levels of wax esters are found in epipelagic fish species, they are mainly stored in roe and the body lipids of these fish

TABLE 1.5 A list of the 24 species under the family Gempylidae

	Species name	Common name	Remarks[a]
1	*Diplospinus multistriatus*	Striped escolar	
2	*Epinnula magistralis*	Domine	Consumed as food
3	*Gempylus serpens*	Snake mackerel	Sold frozen, as sausages or fish cake
4	*Lepidocybium flavobrunneum*	Escolar	Flesh oily and may have purgative properties
5	*Nealotus tripes*	Black snake mackerel	
6	*Neoepinnula americana*	American sackfish	
7	*Neoepinnula orientalis*	Sackfish	
8	*Nesiarchus nasutus*	Black gemfish	Consumed as food
9	*Paradiplospinus antarcticus*	Antarctic escolar	Of no fishery interest
10	*Paradiplospinus gracilis*	Slender escolar	Limited distribution near Namibia and western South Africa
11	*Promethichthys prometheus*	Roudi escolar	Reports of ciguatera poisoning
12	*Rexea alisae*	N/A	
13	*Rexea antefurcata*	Long-finned escolar	A bycatch of deep-water prawn trawl fishery in Australia
14	*Rexea bengalensis*	Bengal escolar	
15	*Rexea brevilineata*	Short-lined escolar	
16	*Rexea nakamurai*	Nakamura's escolar	
17	*Rexea prometheoides*	Royal escolar	Utilized as a food
18	*Rexea solandri*	Silver gemfish	Good edible quality and especially tasty when smoked

(*continued*)

TABLE 1.5 (*continued*)

	Species name	Common name	Remarks[a]
19	*Rexichthys johnpaxtoni*	Paxton's escolar	
20	*Ruvettus pretiosus*	Oilfish	The flesh is very oily, with purgative properties
21	*Thyrsites atun*	Snoek	Highly commercial, marketed fresh
22	*Thyrsitoides marleyi*	Black snoek	
23	*Thyrsitops lepidopoides*	White snake mackerel	Rarely caught since 1980. Good for smoked fish and fish and chips
24	*Tongaichthys robustus*	Tonga escolar	

[a] According to information listed in FishBase (2008).

have no or negligible levels of wax esters. Wax esters, however, are stored in the muscle and other body tissues in deep-sea fish. Wax esters have lower specific gravities than triacylglycerols, and their viscosities are much less influenced by temperature and pressure variations; these properties make wax esters superior to triacylglycerols or the presence of a swim bladder for buoyancy control in deep-sea fish. Therefore, it is not unusual to find high levels of wax esters in deep-sea fish. For example, orange roughy, which is a deep-sea species with high levels of wax esters (Table 1.6) (90–97% of total lipids), is commonly available in the market (Fig. 1.15). Wax esters are mainly found in the skin of orange roughy, and the removal of skin and superficial flesh (deep skinning) significantly reduces the amount of oil present. However, deep-skinned orange roughy still contain 5.5% total lipids of which as much as 93% is indigestible wax esters (de Koning, 2005). Ruello (2004) mentioned that an informant had oily discharge after eating orange roughy, and he himself experienced mild keriorrhea 38 and 60 h after consuming 300 g of this fish. A note was published in the *Hong Kong Medical Journal* to alert the medical professionals to this fish when dealing with sensitive patients (But *et al.*, 2008). In Myctophidae (lantern fish family), many members contain large amounts of wax esters in the body (Table 1.6). Species in this family are well-known for their diel vertical migrations, traveling between 10 m (at night) to 3000 m (at day time), and they are abundant and small in

TABLE 1.6 Wax ester-containing fish species

Family[a]	Species name [valid name][b]	Body part analyzed[c]	Wax esters (% of total lipid)	References
Arripidae	*Armpits trutta* [*Arripis trutta*]	Roe	26	Bledsoe *et al.* (2003)
Bathylagidae	*Bathylagus antarcticus*	Muscle	5	Reinhardt and van Vleet (1986)
Carangidae	*Seriola aureovittata* [*Seriola lalandi*]	Roe	42	Joh *et al.* (1995)
Chlamydoselachidae	*Chlamydoselachus anguineus*	Liver	58	Shimma and Shimma (1970)
Coryphaenidae	*Coryphaena hippurus*	Roe	36	Lee and Patton (1989)
Gadidae	*Melanogramus aeglefinus* [*Melanogrammus aeglefinus*]	Roe	15	Bledsoe *et al.* (2003)
Gempylidae	*Lepidocybium flavobrunneum*	Muscle	89	Matsumoto *et al.* (1955), Nevenzel *et al.* (1965), Mori *et al.* (1966c)
	Ruvettus pretiosus	Muscle	92	Cox and Reid (1932), Nevenzel *et al.* (1965), Mori *et al.* (1966c)

(*continued*)

TABLE 1.6 (*continued*)

Family[a]	Species name [valid name][b]	Body part analyzed[c]	Wax esters (% of total lipid)	References
Gonostomatidae	*Cyclothone acclinidens*	Whole body	29	Lee and Patton (1989)
	Cyclothrone ataria	Whole body	70	Kayama and Nevenzel (1974)
	Cyclothrone pallidae [*Cyclothone pallida*]	Whole body	22	Lee and Patton (1989)
	Cyclothrone pseudopallidae [*Cyclothone pseudopallida*]	Whole body	17	Lee and Patton (1989)
	Cyclothrone signata	Whole body	33	Lee and Patton (1989)
	Gonostoma gracile [*Sigmops gracilis*]	Whole body	20	Kayama and Nevenzel (1974)
Howellidae	*Howella* sp.	Whole body	16	Patton *et al.* (1977)
		Muscle	93	
Latimeridae	*Latimeria chalumnae*	Adipose tissue	97	Nevenzel *et al.* (1966)
Lotidae	*Lota lota*	Roe	80–85	Kaitaranta and Ackman (1981)
Lutjanidae	*Lutjanus campechanus*	Roe	18	Lee and Patton (1989)
Merlucciidae	*Macruronis novaezelandiae* [*Macruronus novaezelandiae*]	Roe	32	Bledsoe *et al.* (2003)
	Merluccius capensis	Roe	25	Mori and Saito (1966a)
	Merluccius hubbsi	Roe	28	Mendez *et al.* (1992)

Moridae	*Laemonema morosum*	Muscle	50	Komori and Agawa (1954, 1955), Ueno *et al.* (1955)
	[*Laemonema longipes*]	liver	60	
	Lotella phycis	Liver	30	Komori and Agawa, (1953)
	Podonema longipes [*Laemonema longipes*]	Liver	25	Hayashi and Yamada (1976)
	Pseudophycis bacchus [*Pseudophycis bachus*]	Roe	26	Bledsoe *et al.* (2003)
Mugilidae	*Mugil cephalus*	Roe	67	Iyengar and Schlenk (1967), Spener and Sand (1970)
	Mugil japonicus [*Mugil cephalus*]	Roe	70	Mori and Saito (1966a)
Myctophidae	*Benthosema glaciale*	Whole body	55	Lee and Patton (1989)
	Centrobranchus chaerocephalus	Whole body	15	Patton *et al.* (1977)
	Electrona antarctica	Muscle	62	Reinhardt and van Vleet (1986)
	Electrona carlsbergi	Whole body	7	Reinhardt and van Vleet (1986)
	Gonichys barnesi [*Gonichthys barnesi*]	Whole body	12	Patton *et al.* (1977)
	Gymnoscopelus braueri	Whole body	61–90	Phleger *et al.* (1999)
	Gymnoscopelus nicholsi	Muscle	20	Reinhardt and van Vleet (1986)

(*continued*)

TABLE 1.6 (*continued*)

Family[a]	Species name [valid name][b]	Body part analyzed[c]	Wax esters (% of total lipid)	References
	Krefftichthyes anderssoni [*Krefftichthys anderssoni*]	Whole body	56–94	Phleger *et al.* (1999)
	Lampanyctus ritteri [*Nannobrachium ritteri*]	Muscle	87	Nevenzel *et al.* (1969)
	Myctophum nitidulum	Whole body	12	Patton *et al.* (1977)
	Neocyttus helgae	Muscle	30	Bakes *et al.* (1995)
	Neocyttus rhomboidalis	Muscle	22	Bakes *et al.* (1995)
	Oreosoma atlanticum	Muscle	9	Bakes *et al.* (1995)
	Protomyctophum bolini	Muscle	8	Reinhardt and van Vleet (1986)
	Stenobrachius leucopsarus	Muscle	90	Nevenzel *et al.* (1969)
	Symbolophorus evermanni	Whole body	10	Nevenzel *et al.* (1969)
	Triphoturus mexicanus	Muscle	74	Nevenzel *et al.* (1969)
Nomeidae	*Cubiceps gracilis*	Whole body	47	Lee and Patton (1989)
Notosudidae	*Scopelosaurus* sp.	Whole juvenile	22	Lee and Hirota (1973)
Nototheniidae	*Pleuragramma antarcticum*	Muscle	48	Reinhardt and van Vleet (1986)

Oreosomatidae	*Allocyttus niger*	Muscle	52	Bakes *et al*. (1995)
	Allocyttus verrucosus	Muscle	76	Mori *et al*. (1966b)
Paralepididae	*Pseudocyttus maculates*	Muscle	62	Bakes *et al*. (1995)
	Paralepsis rissoi [*Arctozenus risso*]	Muscle	85	Ackman *et al*. (1972)
Percidae	*Perca fluviatilis*	Roe	80–85	Kaitaranta and Ackman (1981)
Rachycentridae	*Rachycentron canadum*	Roe	36	Lee and Patton (1989)
Sciaenidae	*Cynoscion nebulosus*	Roe	40	Iyengar and Schlenk (1967)
Scombridae	*Euthynnus alletteratus*	Roe	31	Lee and Patton (1989)
	Scomber australasicus	Roe	26	Bledsoe *et al*. (2003)
Sternoptychidae	*Argyropelecus hawaiiensis* [*Argyropelecus sladeni*]	Whole body	41	Lee and Hirota (1973)
Stomiidae	*Astronesthes* sp.	Whole body	20	Patton *et al*. (1977)
	Eustomias sp.	Whole body	10	Lee and Hirota (1973)
Tetragonuridae	*Tetrogonurus cuvieri* [*Tetragonurus cuvieri*]	Whole body	40	Lee and Patton (1989)
Trachichthyidae	*Hoplostethus gilchristi* [*Hoplostethus atlanticus*]	Muscle	97	Mori *et al*. (1978)
	Hoplostethus islandicus [*Hoplostethus atlanticus*]	Muscle	90	Kaufmann and Gottschalk (1954)

Part of the table modified from Lee and Patton (1989, Table 1) with updated information.

[a] According to information listed in FishBase (2008).

[b] Species name cited as the one listed in the original literature, valid name is based on FishBase (2008).

[c] Whole body included the whole specimen, but some studies excluded guts to eliminate lipids in food.

FIGURE 1.15 Orange roughy fillet retailed in Hong Kong (photo provided by authors).

size (FishBase, 2008). They are occasionally found in fish markets. Other deep-sea fish families that have high levels of wax esters in their muscle, such as Oreosomatidae (oreo family) and Gonostomatidae (bristlemouth family), are mostly of limited fishery interest (FishBase, 2008).

The predominant lipid components in fish roes, like muscles, are triacylglycerols or phospholipids. Yet certain fish species have high levels of wax esters in their roes but not in muscles (Table 1.6) (Bledsoe *et al.*, 2003). Wax esters are present in the roe oil, but not in other muscle and intestine tissues in amber fish (*Seriola aureovittata*) (Joh *et al.*, 1995). Wax esters are specifically located in mullet roes (*Mugil caphalus*) and nowhere else in the fish (Lyengar and Schlenk, 1967). The wax esters in roes, like those in muscles, may play a role in buoyancy, permeability control, insulation, or as an energy reserve (Kaitaranta and Ackman, 1981). However, these wax esters may also be, specifically in roe, acting as a fatty acid reservoir for modifying structural lipids after fertilization (Bledson *et al.*, 2003). The functional differences between the wax esters in muscles and roes could be attributed to the structural differences of wax esters in roes, in which a much higher content of PUFA are present in roes in comparison to those in muscles (Iyengar and Schlenk, 1967; Kalogeropoulos *et al.*, 2008). Indeed, fish roes, such as mullet roes, has long been consumed (Bledson *et al.*, 2003; Kalogeropoulos *et al.*, 2008) and the roes from escolar and oilfish are advertised as high-priced souvenirs from Tungkang, Taiwan (Fig. 1.4). However, the high level of wax esters in these fish roes may cause keriorrhea if too much is consumed.

C. Diacylglyceryl ether (DAGE)-rich fish

It was reported in Japan that students in a primary school suffered diarrhea and oil leakage after consumption of *Stromateus maculatus* (Iida, 1971; Sato *et al.*, 2002). Sato *et al.* (2002) analyzed the lipid composition of *S. maculatus* and found DAGE as the major lipid class in muscle (55% of total lipids), but no wax ester was detected. They further conducted an acute toxicity test and found dose-dependent toxicity responses. On day 2 of administration, the results showed significant reduction in body weight (4.4 $\pm$ 1.7 g), high diarrhea rate (43%), and high mortality rate (4/7) in mice given DAGE equivalent to 1/40 of their body weight. The toxicity was even higher when DAGE and triacylglycerol was given together. However, this dose is equivalent to 0.43 g of DAGE in a mouse of 17 g and 1.5 kg of DAGE in a man of 60 kg. The dose tested is far beyond normal human consumption.

DAGE is widely distributed in various fish (Mori *et al.*, 1972). Some fish, however, possess extraordinary high levels of DAGE in their muscles (Table 1.7) (Endo *et al.*, 2001; Iida, 1971; Mori *et al.*, 1972; Nichols *et al.*, 2001; Sato *et al.*, 2002). DAGE is likely used in deep-sea fish to achieve buoyancy (Endo *et al.*, 2001). Little is reported on the toxicity of DAGE. Capsules of DAGE derived from the livers of deep sea dogfish, however, are widely marketed as neutraceuticals for human consumption (Nichols *et al.*, 2001).

DAGE is not wax. In a strict sense, DAGE excretion should not be classified as keriorrhea, which is coined specifically for wax excretion, and thus is beyond the coverage in this review. Further studies, however, are recommended concerning *Stromateus maculatus* and its DAGE-rich lipid and possible incidences of illness. If a broader descriptive is needed for medical description of oil leakage including wax esters and other oils, ladiorrhea, where ''ladi'' stands for oil in Greek, can be used.

TABLE 1.7 Diacylgylceryl ether (DAGE)- or gylceryl ether (GE)-rich fish species

Family	Species name	DAGE/GE (% of total lipid)	References
Centrolophidae	*Centrolophus niger*	14.7–92.5	Nichols *et al.* (2001)
	Centrolophus sp.	27.7	Mori *et al.* (1972)
	Tubbia sp.	2.2–82.1	Nichols *et al.* (2001)
Nomeidae	*Cubiceps gracilis*	25.4	Mori *et al.* (1972)
Stromateidae	*Stromateus maculatus*	20.3	Mori *et al.* (1972)

VII. DISCUSSION AND RECOMMENDATIONS

A. The rationale: To ban or not to ban?

The incidence of keriorrhea is unlike other food-poisoning cases. Only some people have a reaction after eating the fish. Escolar and oilfish have been traditionally used for food and as a purgative medicine (Cox and Reid, 1932; Gudger, 1925; Gudger and Mowbray, 1927; Helfman *et al.*, 1999; Raisfeld and Patronite, 2006; Ruiz-Gutierrez *et al.*, 1997; Stobbs and Bruton, 1991). Some connoisseurs of good foods even gave them high compliments as dream foods (Bykov, 1983; Raisfeld and Patronite, 2006). Their flesh and roes are regarded as a delicacy in Taiwan (Li, 2007).

Despite the shocking animal study that saw 13 out of 16 rats fed daily with high doses of escolar or oilfish die within 10 days (Mori *et al.*, 1966c), it is very unlikely that normal human consumption at any single time could be life-threatening. Indeed, the responses to eating the fish are highly variable and unpredictable due to differences in individual susceptibility and variation in wax ester content between servings. However, the rationale is that people do not all tolerate the same food in the same manner, and some people may have medical conditions, such as food allergies, that preclude them from consuming certain items. Therefore, countries that consider the two fish dangerous and ban them should check fish on the market constantly to avoid illegal sale, while countries that consider the two fish safe should check for mislabeling to ensure that people know what they consume and, at the same time, require a proper warning sign be shown. In either case, food safety is of utmost concern whether the fish is banned or not. The highest food safety standards can be achieved through education and inspection, together with appropriate penalties that deter either illegal sale or mislabeling.

B. Recommendations

1. Labeling

The problem of misidentification and mislabeling of escolar and oilfish occurs throughout the entire supply chain. Escolar and oilfish are named differently in different places. Moreover, the fish are mislabeled differently across countries, for example, as butterfish and rudderfish in Australia and as sea bass in Britain. In response to keriorrhea outbreaks, a technical advisory group was established in Australia to assist the fishing industry and consumers in identification and labeling. The common names of ''escolar'' and ''oilfish'' are endorsed for *L. flavobrunneum* and *R. pretiosus*, respectively. The advisory group also distributed pictures of fish species responsible for keriorrhea to the industry and included both fish in the Australian Seafood Handbook. Similarly, the Hong Kong Centre for Food Safety issued Guidelines on Identification and Labeling of Oilfish/Cod with a view to regulating the naming, labeling and handling of the two fish (hereafter known as HK Guidelines; WGNCO, 2007). In the HK Guidelines, retailers are advised to indicate designated common names on their packages, in which case *R. pretiosus* and *L. flavobrunneum* should both be labeled as ''oilfish'' and no other names are allowed. In Britain, both *L. flavobrunneum* and *R. pretiosus* are labeled the same as ''escolar'' according to UK Food Standards Agency. To facilitate a proper communication between authorities in different countries, standard common names should be designated for *L. flavobrunneum* and *R. pretiosus*, as has occurred in Australia.

2. Risk assessment and education

Many food science and public health professionals are not well-informed of fish-induced keriorrhea. The public and health professionals should be educated on the potential health threat related to exotic food, such as escolar and oilfish. User-friendly brochures or leaflets are useful to the general public, especially vulnerable groups including pregnant women and people suffering from cardiovascular and gastrointestinal illness, on the possible consequences arising from escolar and oilfish consumption. After all, well-informed consumers are less likely to panic once affected and in turn, they could better describe their symptoms and take proper action, such as seeking help and reporting to pertinent authorities, once symptoms are noted. A prompt response to any keriorrhea outbreak allows physicians and sensitive consumers to be alerted to possible hazards and facilitates rapid diagnoses. Time is an essence to the problem before it becomes widespread. The seafood and catering industry is another key player in preventing such outbreaks from becoming more prevalent. Industry should be educated on identifying problematic fish and use correct seafood names with proper labels and warning signs. Moreover, the catering industry should be educated on the appropriate manner to handle the fish so as to reduce the level of offensive wax esters and to avoid bacterial growth, which will lead to scrombrotoxin. In short, any education program needs to include the industry, consumers, health professionals, and food safety agencies in order to establish a social norm for appropriate preventive and remedial measures.

3. Warnings and handling

In countries where escolar and oilfish are not banned from sale, the display of warnings and proper handling procedures should be made compulsory whenever the fish are available. In the HK Guidelines (WGNCO, 2007), retailers are advised to display supplementary warning statements, such as: (i) this fish can cause digestive discomfort to some individuals; (ii) if you are pregnant, have bowel problems, or malabsorption, you are advised not to consume this fish; (iii) if you are eating this fish for the first time, consume only a small portion; (iv) if you experience gastrointestinal symptoms after eating this fish, do not consume the fish in future; and (v) seek medical advice if symptoms persist. Both British (Food Standards Agency) and Singaporean (Agri-Food and Veterinary Authority) authorities recommend cooking methods, such as grilling, in order to reduce the oil content. In 1999, the Swedish and the Danish National Food Administrations required cooking recommendations, including cooking these fish in such a way that most of the fat could be separated from the dish and the cooking liquid must not be used for preparation of sauce, to be available where the fish are offered for sale (Alexander *et al.*, 2004). Ruello (2004), however, did not find much difference by grilling or baking. Moreover, people are advised to remove or avoid sucking the bones because of their notably high oil content (Nordhoff, 1928). It was also recommended to keep the storage time short because of the high content of histidine (Alexander *et al.*, 2004).

For health professionals in consultations with patients complaining of diarrhea, it is pertinent to ask ''Is it oily?'' and ''Have you consumed fish?'' If answers are confirmative, the case should be reported to food inspection agencies. To follow up on the alert, food inspection agencies should collect the expelled oil sample, a residual sample of the cooked fish (if available), and any uncooked fish from the same source to check for wax esters. If wax esters are detected, DNA analysis should be applied, if possible, to identify the source species. Concurrently during the inspection process, food safety agencies should trace back to the supply source of the fish to see if proper labels were in place. If not, warnings should be issued to the public, healthcare professionals and fishery industry.

4. Detection and inspection

Any sound policy needs proper inspection to facilitate implementation. A good authentication method is clearly necessary to check against substitution, misidentification, and mislabeling. This is particularly important at an initial stage of a keriorrhea outbreak, to stop further circulation of incriminated samples at outlets and sources and to prevent the situation from escalating- to political uproar. The recent situation in Hong Kong was illuminating. In fall 2006, oilfish cutlets were labeled as codfish but at lower prices. Initially, scattered cases of keriorrhea and other complaints surfaced through the mass media. In response to public inquiry, the agency responsible for food monitoring merely advised citizens to buy from reliable sources and recommended the public to be cautious in purchasing fish. That recommendation could hardly curb the spread of keriorrhea and soon over 600 cases were recorded by mid-January 2007. The general public in Hong Kong was panicking and various political parties organized demonstrations demanding for proper government actions (Fig. 1.16). To help round up mislabeled items and offer a tool to the fish industry, the team led by the senior author announced in early February 2007 a rapid TLC detection method validated by molecular sequencing and GC-MS (Goh, 2007; Ling *et al.*, 2008a,b). The uproar then subsided.

Authentication methods, including morphological, anatomical, protein, DNA, and lipid analyses, can be utilized in differentiating escolar and oilfish from other commonly marketed fish. Accuracy is of utmost importance. Cost and time are also important factors in screening large numbers of fish samples, either for routine inspection or after an outbreak. The simple, rapid, and inexpensive TLC method developed by Ling *et al.* (2008a,b) serves as a good example for differentiating escolar and oilfish from other commonly marketed fish, which contain no wax ester. It is applicable to cooked or excreted samples as wax esters are heat-stable and indigestible by humans. The whole process, from lipid extraction to staining, took less than 30 min while the equipment involved is readily available in most analytical laboratories. Because each TLC plate can accommodate more than 20 samples, and multiple plates can be run simultaneously, the method is space-saving and suitable for screening large sample sets. The method, however, cannot distinguish escolar from oilfish nor differentiate the two fish from other wax ester-containing fish. Other more thorough protocols, such as DNA sequencing, can be the next step in confirming the precise sample identity.

FIGURE 1.16 Demonstration demanding immediate government actions against oilfish-induced keriorrhea epidemic in Hong Kong (photo of the Democratic Alliance for the Betterment and Progress of Hong Kong, reprinted with permission).

VIII. CONCLUSIONS

The escolar- and oilfish-related problems are global in scope and respect no national boundaries. Differences in opinions, lack of clinical data, confusing labeling systems, and expensive detection methods are all factors that have contributed to the prevalence of the problem over decades. Albeit the uncertainty, like playing Russian roulette, it is clear that some people consume the fish without any notable response while some others experience serious keriorrhea. It is important to regulate the fish, either by complete banning or designated labeling, and educate the general public for the potential risks regarding escolar and oilfish consumption. Keriorrhea is likely not restricted to escolar and oilfish, and other wax ester-rich fish, known or unknown, may also pose a threat to consumers. It is therefore crucial to inform health professions of the distinctive symptoms of expelled oil droplets. Lastly, the academia and research agencies should continue to investigate the lipids of various fish for the possible identification of those species with unusually high content of wax esters, given that fish are the largest group of vertebrates and a significant part of human diet.

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