Endosulfan: Its Isomers and Metabolites in Commercially Aquatic Organisms from the Gulf of Mexico and the Caribbean

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Abstract

The organochlorine pesticide endosulfan is an insecticide and acaricide used on a variety of crops around the world. Its adverse effects on public health and aquatic biota have been widely documented in several studies, which are closely related to their primary route of exposure, by eating food contaminated with this compound. Therefore, it is necessary to concentrate the information in order to analyze and understand its impact on public health. The present objective is to review the characteristics of endosulfan, its isomers and their presence in aquatic organisms of commercial importance in the Gulf of Mexico and the Caribbean. The aquatic organisms involved were molluscs, crustaceans and fish. The highest concentrations of endosulfan have been detected in oysters, *Crassostrea virginica*, with a maximum value of 99.48 ± 16.21 ng g^{-1}. Although the use of this insecticide for pest control worldwide is prohibited, research conducted in the Gulf of México and Caribbean Sea indicate that it is still used, which will affect future public health and consumers.

Keywords: benthic organisms, bioaccumulation, biomarker, isomers, organochlorine

1. Introduction

The organochlorine pesticide endosulfan (3-oxide 6, 9-methano-2, 4, 3-benzodioxatiepina-6, 7, 8, 9, 10, 10-hexachloro-1, 5, 5a, 6, 9, 9-hexahydro) is considered a persistent organic pollutant (POP) due to its chemical characteristics and effects on public health and the environment (UNEP, 2009a). This pesticide is a high-risk pollutant to the environment, particularly in coastal aquatic environments due to its different transport routes including runoff and atmospheric deposition (Albert & Benítez, 1996; Albert, 2014).

In 1950, the German companies Hoechst AG and FMC *Corporation* first introduced this pesticide to be used on crops such as cereals, coffee, tea, fruits, vegetables, tobacco and cotton (Maier-Bode, 1968). In general, the trends for the total global endosulfan used and the total global emissions have increased continuously ever since the first year of application of it. Currently, total emissions are around 150 kilotons (Y. F. Li & D. C. Li, 2004; Li & Macdonald, 2005). Despite its widespread use in many countries, at least in 60 it is prohibited due to its high toxicity that affects public health and aquatic organisms, and due to its persistence in the environment (PANAP, 2009; Bauer et al., 2013; Negro et al., 2013; Aly & Khafagy, 2014; Schmidt et al., 2014).

The composition of the technical grade of endosulfan corresponds to a diastereomeric mixture of two biologically active isomers, alpha (α) and beta (β), with an approximate ratio of 2:1 to 7:3, in addition to impurities and degradation products (INIA, 1999; INE, 2011; UNEP, 2011). The appearance of this compound, as a solid, corresponds to cream or brown-colored crystals or flakes, whose existence does not occur naturally in the environment (ATSDR, 2000, 2001, 2013). As a technical grade product, it must contain at least 94% endosulfan according to the United Nations for Food and Agriculture (FAO Specification 89/TC/S), which stipulates that the alpha-isomer content is between 64 and 67% and the beta-isomer is between 29 to 32%. The alpha-isomer is asymmetric and is composed of two axial seat forms, while the beta-isomer has a symmetric shape. The beta-isomer is easily converted into endosulfan-alpha, while this is not possible for the alpha-isomer

(INIA, 1999; INE, 2011).

Due to the high negative impact of endosulfan and its isomers on public health and the environment, several investigations have been conducted with the objective of replacing this organochlorine in both Latin America and Europe (IPEN, 2005; Bejarano et al., 2008, 2009; Haffmans et al., 2008; UNEP, 2008). Thus, it is important to know the concentration levels of endosulfan and its isomers in commercially important aquatic organisms in the Gulf of Mexico and the Caribbean, and the possible risk to public health.

2. Primary Crops and Pests Controlled by Endosulfan

Endosulfan is an insecticide and acaricide used to control plant pests (Li & Macdonald, 2005; UNEP, 2009a). It is a broad spectrum compound applied in different countries to a variety of edible and non-edible crops (Table 1).

Table 1. Tropical crops and pests of economic importance controlled by the application of endosulfan

Family	Crop	Pest	
		Scientific name	Common name
Ribiaceae	Coffee	*Hypothenemus hampei* Ferrari	Coffee berry borer
Solanaceae	Tomato	*Trialeurodes vaporariorum* (Westwood)	Whitefly
	Mexican green tomato	*Aphis*	Aphids
		Manduca quinquemaculata (Haworth)	Hornworm
		Helicoverpa zea (Boddie), *Heliothis virescens* (Fabricius)	Fruit and sprout worms
		Trichoplusia ni (Hübner)	Looper
	Eggplant	*Myzus persicae* (Sulzer)	Aphids
		Phyllotreta, Epitrix	Fleahopper
		Helicoverpa zea, H. virescens	Fruit and sprout worms fruit and sprouts
	Hot pepper	*Anthonomus eugenni* Cano	Hot pepper borer
		Epitrix, Chaetocnema	Fleahopper
		Trialeurodes vaporariorum	Whitefly
		Acyrthosiphon pisum (Harris)	Green aphid
	Tobacco	*Bemisia tabaci* (Gennadius)	Whitefly
		Heliothis virescens	Tobacco sprout borer
		Estigmene acrea (Drury)	Hairy worm
		Alabama argillacea (Hübner)	Looper
		Myzus persicae	Aphids
Fabaceae	Alfalfa	*Therioaphis maculata* (Buckton)	Spotted aphid
		Acyrthosiphon pisum	Aphid
		Melanopus, Sphenarium, Brachystola	Grasshoppers
		Hypera brunneipennis (Boheman)	Egyptian weevil
	Green beans	*Acrythosiphon pisum*	Green aphid
		Trichoplusia ni	Looper
		Empoasca	Leafhoppers
	Beans	*Apion godmani* Wagner	Bean weevil
		Trialeurodes vaporariorum	Whitefly
		Empoasca	Leafhoppers
	Soy	*Anticarsia gemmatalis* Hübner	Soy or velvet caterpillar
		Bemisia tabaci, B. argentifolii Bellows & Perring	Whitefly
		Schistocerca piceifrons piceifrons Walker	Locust
		Nezara viridula (L.)	Green bug
		Euschistus servus (Say)	Brown bug or Brown cochuela
Malvaceae	Cotton	*Anthonomus grandis*	Boll weevil
		Heliothis virensis	Acorn worm
		Trichoplusia ni	Looper

		Bemisia tabaci, T. vaporariorum	Whitefly
		Aphis gossypii (Glover)	Cotton aphid
Apiaceae	Celery	*Lygus*	Lygus bug
Brassicaceae	Broccoli	*Trichoplusia ni*	Looper
	Cabbage	*Pieris rapae* (L.), *Pontia protodice* (Boisduval & Leconte), *Leptophobia aripa* (Boisduval)	White cabbage butterfly
			Diamondback moth
		Plutella xylostella (L.)	Cabbage aphid
		Brevicoryne brassicae (L.)	Harlequin Cabbage Bug
		Murgantia histrionica (Hahn)	Looper
		Trichoplusia ni	
	Cauliflower	*Epitrix, Phyllotreta*	Fleahopper
		Spodoptera exigua (Hübner)	Armyworm
		Trichoplusia ni	Looper
Poaceae	Sugarcane	*Aeneolamia postica* (Walker) Fennah, *Prosapia bicincta* (Say), *P. simulans* (Walker)	Spittlebug
			Stem worm borer
		Eoreuma loftini (Dyar), *Diatraea considerata* Heinrich, *D. grandiosella* Dyar	Yellow aphid
		Sipha flava (Forbes)	Lace bug
		Leptodyctia tabida (Herrich-Schaeffer)	
	Corn	*Spodoptera frugiperda* (J.E. Smith), *Rhopalosiphum maidis* (Fitch)	Bud aphid
			Foliage aphid
		Schizaphis graminum (Rondani)	Pink borer
		Sesamia calamistis Hampson, *S. inferens* (Walker)	Stem worm borer
		Diatraea grandiosella, D. lineolata (Walker)	Corn worm
		Helicoverpa zea	
	Wheat	*Diuraphis noxia* Kurdjumov	Russian wheat aphid
		Rhopalosiphum maidis	Aphid bud
		Schizaphis graminum	Foliage aphid
		Sitobion avenae Fabricius	Grain aphid
		Sesamia calamistis	Pink borer
	Rice	*Orseolia oryzae* Wood-Mason	Gill fly
		Euetheola bidentata Burmeister	Hispid or rice louse
		Rupela albinella Becker & Solis	Stem worm
	Barley	*Rhopalosiphum maidis*	Aphid bud
		Sitobion avenae	Grain aphid
	Pasture	*Aeneolamia postica, Prosapia simulans*	Whitefly
		Macrodactylus	Puffin
		Dalbulus elimatus (Ball)	Leafhopper
		Sphenorium, Melanoplus	Grasshoppers
Asteraceae	Lettuce	*Trichoplusia ni*	Looper
		Epicaerus cognatus Sharp	Potato weevil
		Aphididae	Aphids
		Epitrix	Fleahopper
		Leptinotarsa decemlineata (Say)	Catarina potato
Cucurbitaceae	Zucchini	*Aphis gossypii*	Melon aphid
	Melon	*Trichoplusia ni*	Looper
		Diaphania nitidalis (Stoll), *D. hyalinata* (L.)	Fruit borer
		Melittia satyrinfornis Hübner	Guide borer
		Bemisia tabaci, Trialeurodes	Whitefly
	Cucumber	*Trichoplusia ni*	Looper
	Watermelon	*Aleyrodidae*	Whitefly
		Aphis gossypii	Cotton aphid
Bromeliaceae	Pineapple	*Thecla basilides* (Harris)	Pineapple borer

| | | *Dysmicoccus brevipes* (Cockerell) | Mealy louse |
| Anacardiaceae | Mango | *Anastrepha ludens* (Loew) | Fruit fly |

Sources: Nieto (2001), EPA (2002), Bejarano et al. (2008, 2009), Weber et al. (2010), UNEP (2009b, 2011), ATSDR (2013), TecnoAgro (2013), Pro-Agro (2014a, 2014b).

The extensive use of pesticides in a wide variety of crops has contributed to their release into the environment (FAO, 2000). The irrigation systems are an example of the mechanisms of modern agriculture that have contributed to a more efficient spreading of fertilizer and pesticides like endosulfan, where the former have generated pollution of groundwater with nitrates and nitrites by overuse mode (Galaviz et al., 2010). Meanwhile, the pesticides applied using these systems can influence the transport of these compounds, which are in use or previously used as the organochlorine, helping to transport to remote areas like the lagoon systems.

Knowledge about the status of irrigation systems at global and national level is of importance for present and future transport of pesticides like endosulfan. Among the most recent works on this subject are those by Valipour (2012, 2014a, 2014b, 2014c, 2015). In addition, this author indicated that irrigation systems in any crop should be implemented to achieve sustainable agriculture in the future.

3. Route of Exposure to Endosulfan

Due to the non-systemic nature of endosulfan, the major route of action occurs through direct skin contact and ingestion (Kidd & James, 1991). It is a very toxic chemical for nearly every type of organism (UNEP, 2007). Endosulfan and its degradation by products are also highly toxic to aquatic organisms (UNEP, 2011). Exposure occurs by absorption through contact, inhalation and ingestion (Nieto, 2001).

Diet is the primary route of exposure to endosulfan for most organisms resulting from food contaminated by this compound (ATSDR, 2013; Singh et al., 2014; Wang et al., 2014). In rats, rapid absorption of it occurs in the gastrointestinal tract at levels from 60% to 87%; where 60% of this compound is absorbed within 24 hours (UNEP, 2011).

4. Effect of Endosulfan on Public Health

Major impact to public health by endosulfan is the nervous system damage due to its affinity to gamma-aminobutyric acid receptors (GABA) in the brain, where it acts as a noncompetitive antagonist of GABA, blocking or inhibiting neurotransmitter reception. Therefore, the blocking activity means partial repolarization of the neuron and a state of uncontrolled excitation (UNEP, 2011). Exposure to high concentrations of this compound produces hyperactivity and seizures, regardless of the route of exposure. Symptoms of acute poisoning include vomiting, agitation, convulsions, cyanosis, dyspnoea, foaming at the mouth and noisy breathing. Severe poisoning can cause death. Furthermore, animal research has shown that prolonged ingestion of endosulfan in food mainly affects kidneys (Bejarano et al., 2009; Scremin et al., 2011; UNEP, 2011; ATSDR, 2013).

However, there are conflicting reports; endosulfan has no genotoxic or mutagenic effects *in vitro* or *in vivo* for somatic cells. Neither has it been classified as an endocrine disruptor, or an immunotoxicant, although carcinogenic effects have been observed in studies on mice and rats (Nandar et al., 2011). However, the results obtained in studies of germ cells *in vivo* suggest that mutations could be induced specifically in spermatogonia UNEP (2011).

Recent studies also indicate that endosulfan can cause cell death in exposed Sertoli germ cells due to oxidative damage, causing further damage to the quality of gametes produced (Rastogi et al., 2014). Such contradictions regarding the adverse effects on public health could be related to the limited amount of research performed on humans, as a high percentage of such studies are focused on laboratory animals such as mice, rats, dogs, and other mammals.

Besides, the effect of endosulfan as an endocrine disruptor not only in terrestrial and aquatic species, but also in public health, because this chemical has an estrogenic effect and causes the proliferation of breast cancer cells MCF-7 sensitive to human estrogen, and interferes with male sex hormones such as testosterone (Bejarano et al., 2009). Endosulfan isomers and its primary metabolite have been on the TEDX list of potential endocrine disruptors since 2011, in which is included the evidence that supports the consideration of this chemical as an endocrine disruptor (TEDX, 2015). Study results suggest that exposure to endosulfan in young men can delay sexual maturity and interfere with the synthesis of sex hormones (Saiyed et al., 2003).

In the Kerala state of India, helicopters sprayed endosulfan on nut crops for 25 years, leading to adverse effects

on human health and calves with congenital deformities since 1979. During the 1990s, an unusual increase in health problems was reported in Kasaragod, one district of Kerala. In 2001, more cases of children with hydrocephalus, cerebral palsy, blindness, deformed hands, and chronic skin problems were reported (Bejarano et al., 2008).

Study results on the genotoxicity and mutagenicity caused by this chemical have been equivocal and the genotoxicity of its metabolites is largely unknown. Studies on the damage to human lymphocyte DNA caused by endosulfan isomers has shown that exposure to endosulfan and its metabolites in sublethal doses induces damage to DNA and promotes mutation (Bajpayee et al., 2006). The induction of teratogenic effects by endosulfan in pregnant rats also was tested, showing the number of fetuses with visceral and skeletal malformations to be significantly higher than controls. The malformations obtained were mainly skeletal (ribs), vertebral, and in the liver and kidneys (Singh et al., 2007); it was also observed an effect of the developing chick embryos (Mobarak & Al-Asmari, 2011).

No observable effects levels (NOEL) were established for endosulfan risk assessment during reproductive development and its neurotoxicity. For acute oral exposure in rabbits, 0.7 mg^{-1} kg^{-1} d^{-1}, and for breeding rats, values for subchronic and chronic oral exposure were 1.2 mg^{-1} kg^{-1} day^{-1} and 0.6 mg kg^{-1} d^{-1}, respectively. Silva and Gammon (2009) concluded that endosulfan toxicity during development or reproduction results in endocrine disruption only at doses that cause neurotoxicity (0.5 mg kg^{-1} d^{-1} for rat pups). Risks to human health from endosulfan exposure were assessed using NOELs to compare acute, subchronic and chronic exposure; resulting in 0.7, 1.18 and 0.57 mg^{-1} kg^{-1} day^{-1}, respectively. The acute oral NOEL reported by the EPA was found to be twice as high as reported values (1.5 mg^{-1} kg^{-1} day^{-1}) (Silva & Beauvais, 2010). Silva and Carr (2010) found that children from 1-6 years old have a higher risk of exposure to endosulfan in the diet (Silva & Carr, 2010).

5. Transformation and Transport in the Environment

The primary metabolite obtained from the degradation of endosulfan is endosulfan sulfate, which has the same toxicity of the parent compound (UNEP, 2008). However, the metabolite is even more persistent because it degrades slowly compared to more polar metabolites such as endosulfan diol, endosulfan lactone, and endosulfan ether (Bejarano et al., 2009; UNEP, 2011, 2013). Endosulfan transforms primarily through two channels: the diol route in water and as endosulfan sulfate in soils and sediments (Hose et al., 2003).

The presence of endosulfan residues has been reported in several countries, in all environmental systems studied, including air, rain, snow, fog, lakes, rivers, river sediments, groundwater, well-water, spring-water, city water supplies, seawater and marine sediment, shrimp ponds, lagoons, estuary sediment, soil, and tree bark. In addition, it is reported in biota like aquatic plants, fish, crocodile eggs and several organisms in such remote areas as the Arctic (CE, 2005; Bejarano et al., 2008; Rendon & Bejarano, 2010). Due to its presence in a variety of environments, its degree of persistence varies depending on the environmental system and conditions present. The persistent characteristics for the major environmental systems (air, soil and water) are described below.

In air, endosulfan is stable regarding photolysis, but photooxidation occurs to produce endosulfan sulfate (UNEP, 2011). Therefore, the atmosphere is a major transport route of semi-mobile pesticides such as endosulfan. The deposition of this compound is associated with its physicochemical properties, patterns of use and climatic conditions, on local, regional and global scales. Therefore, endosulfan and its metabolites can affect human health and have adverse ecological effects (Potter et al., 2014). This coincides with what is known about endosulfan as a global pesticide, particularly the persistence of α-endosulfan and its ability to travel great distances through atmospheric transport (UNEP, 2009a). The persistence and volatility of endosulfan contribute to its dissemination in the environment after being applied and its ability to travel great distances, making it the organochlorine with the highest concentration in the atmosphere worldwide (Bejarano et al., 2009; UNEP, 2011; INE, 2011); providing a dispersal distance of 10-20 kilometers for low to moderate use (Gioia et al., 2005), and up to 150 kilometers for regional transportation (Hageman et al., 2006).

Evaluations of endosulfan wet deposition via precipitation in an area of high agricultural use in South Florida and near to the Biscayne and Everglades National Parks, recorded a detection rate of 55-98%, average concentrations between 5-87 ng L^{-1} and a total daily deposition of 200 ng m^{-2} day^{-1}. The compound showed a strong seasonal trend in its concentration, with significantly higher values associated with peak use periods when vegetable crops were grown (Potter et al., 2014). Within an area, the simple intensive aerial application of a pesticide such as endosulfan results in volatile releases to the atmosphere. In addition to regional characteristics, such as calcareous soils, the presence of frequent rainfall, high humidity and temperature help to accelerate the process of regional volatilization (Hapeman et al., 2013).

The levels of total endosulfan (Σ) were analyzed in ambient air in southern Mexico; the highest levels of

α-endosulfan occurred at two sites in Tabasco and one in Veracruz, with an average concentration of 367 and 78 pg m^{-3}, and 83 pg m^{-3}, respectively (Alegría et al., 2005). Mobilization and atmospheric deposition are partly responsible for the presence of organochlorine pesticides in coastal areas and its atmospheric transport at a regional scale (Alegría et al., 2005). A persistence of 27±11 days in the atmosphere (and 75 °C for photolysis) was noted, with a DT$_{50}$ > 2.7 days for the alpha isomer and >15 days for the beta isomer (UNEP, 2008, 2009a). However, neither endosulfan sulfate nor total endosulfan were reported. A persistence of the total composite for a scenario in the United States yielded 1.3 days, while 2 days for Europe was recently indicated; although no explanation for these variations has been provided (INE, 2011).

The persistence of endosulfan in soil is high because it is strongly adsorbed and relatively immobile (Nieto, 2001; Singh et al., 2014). Table 2 shows the persistence of endosulfan and its isomers in soil. Its semidegradation period (DT$_{50}$) varies depending on whether it occurs under aerobic conditions, the region, (temperate or tropical) and the conditions of the land where it was applied. Under aerobic conditions it is estimated that soil and sediment are acidic to neutral. The DT$_{50}$ for total endosulfan (alpha and beta isomers and endosulfan sulfate) ranges from 9 months to 6 years (UNEP, 2009). Persistence also is associated with laboratory or field conditions under studies are conducted. In the laboratory, DT$_{50}$ values < 30 days have been reported, indicating that the persistence of alpha and beta endosulfan in soil is low. Yet, field investigations have indicated DT$_{50}$ values for endosulfan sulfate and the technical grade compound as being 3-8 months (UNEP, 2011).

Table 2. Persistence (DT$_{50}$) of endosulfan and its isomers in soil

Environmental System	Isomers				
	Alfa (α)	Beta (β)	Sulfate	Total (∑)	Reference
Soil	12-39 days	108-264 days	N.D.	7.4 days	CE (2005)
	21 to 22 °C	21 to 22 °C		DT$_{90}$: 24.6 days	
	Acidic to neutral soils, 1-2 months	Acidic to neutral soils, 3 to 9 months	N.D.	288 to 2,241 days	UNEP (2007)
	Average: 27.5 days	Average: 157 days		Tropical soils from Brazil, 161 to 385 days	
	Average: 27.5 days	Average: 157 days	117 to 137 days	9 months to 6 years	Bejarano et al. (2008)
	α+β, laboratory aerobic degradation, 25-128 days		Aerobic degradation	28 to 391 days	UNEP (2009)
	α+β in temperate regions, 7, 4 and 92 days		123-391 days		
	Neutral pH, 35 days	Neutral pH, 150 days	N.D	Acid pH, 50 days	INECC (2014)
	12 to 39 days	108 to 264 days	123 to 391 days	9 months to 6 years	UNEP (2011)
		Field studies: 900 days	Field studies: 3 to 8 months		

Note. N.D. = Not defined.

While, alpha endosulfan has an average DT$_{50}$ of 27.5 days, the beta-isomer an average of 157 days, and endosulfan sulfate 117 to 137 days, anaerobic conditions may considerably extend the semidegradación rate in soils (UNEP, 2007; Ciglasch et al., 2008). However, there is variability among these degradation rates, such that degradation for the α isomers ranges from 12-128 days and for the endosulfan sulfate from 123-391 days (UNEP, 2011). The latter range is similar to reports indicating that the combined DT$_{50}$ for the two isomers (α and β) and endosulfan sulfate in soil varied in the range of 28-391 days (UNEP, 2008).

For aquatic environments, only the persistence for total endosulfan has been determined, and that there is a strong association with pH (hydrolytic degradation). Low pH conditions (pH 5 and lower, acidic) and temperatures near 25 °C promote longer periods of degradation, yielding a DT$_{50}$ > 200 days. Under neutral pH conditions, a DT$_{50}$ of 10 to 20 days exists, but less than a day to 0.2 days at pH 9 (alkali or basic). Among the metabolites obtained during this transformation are endosulfan sulfate, endosulfan diol, endosulfan lactone and endosulfan hydroxy acid (Bejarano et al., 2008; UNEP, 2007, 2011). The relationship between pH and the persistence of total endosulfan indicates that under anaerobic conditions, with an acid pH, persistence was four

days (INECC, 2014). In contrast, a DT_{50} of more than 120 days has been reported, but the authors do not describe the conditions under which this process occurs (UNEP, 2009). As for water-sediment conditions, retention of the compound was 3.3 - 273 days with pH 7; the persistence varied from 10 - 20 days with pH 9 and 25 °C, endosulfan remained for 0.2 days (Jones, 2002, 2003; UNEP, 2007). In summary, the route transport of endosulfan isomers and metabolites from agricultural areas to aquatic systems are described on Figure 1. Endosulfan isomers and metabolite can be found in the atmosphere; however, the α-isomer is more common due to its application results in volatile releases to the atmosphere and the β -isomer is easily converted into α-endosulfan. In soil, β-endosulfan and endosulfan sulfate are more common because they tend to strongly join to sediments. In acuatic environments, endosulfan can be found as α and β isomers, and sulfate and diol metabolites. These two metabolites predominate in this environment. Endosulfan sulfate is more persistent because it degrades slowly.
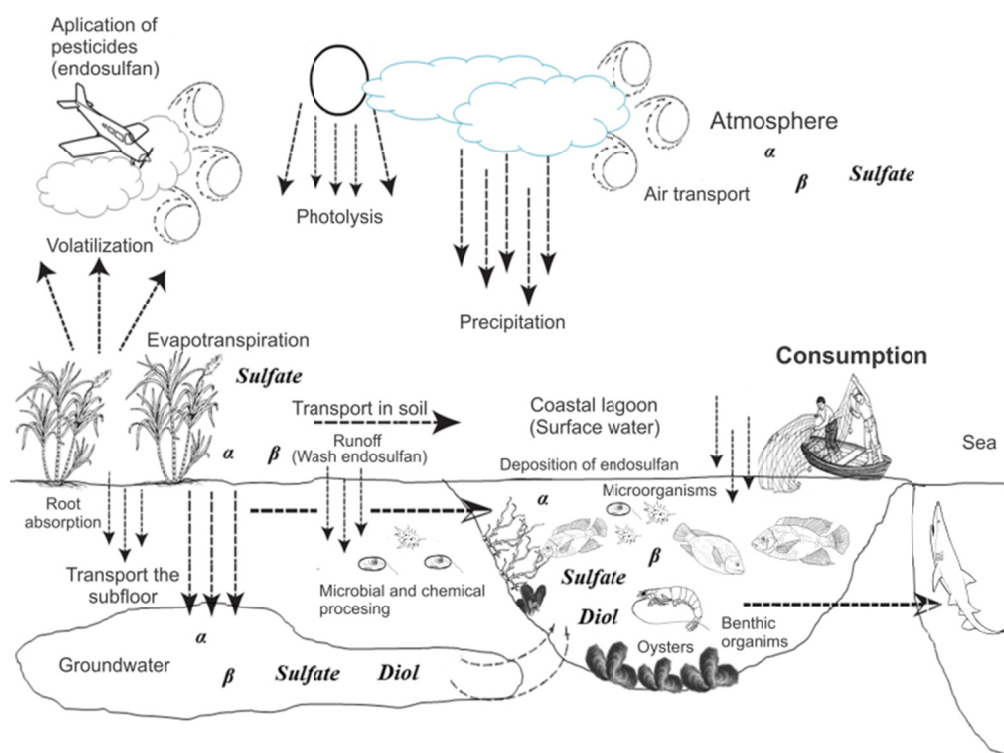

Figure 1. Transport of endosulfan isomers and metabolites from agricultural areas to lagoon systems

6. Permissible Limits of Endosulfan

Because of the toxicological effects related to the presence and use of endosulfan, permissible limits have been established to protect public health and aquatic life. Some of these guidelines are described below. The acceptable daily intake of endosulfan (ADI) is 6 ng g^{-1} day^{-1}, and a reference dose for acute oral exposure (ARfD) is 15 ng g^{-1} day^{-1} (CE, 2005). Levels of endosulfan sulfate in lakes, rivers, streams and bodies must not exceed 62 ng g^{-1} to protect public health against adverse effects from the consumption of water and aquatic organisms (fish and shellfish) from contaminated waters. A limit of 89,000 ng L^{-1} of endosulfan was established (EPA, 2009) for human consumption. Also, EPA (2002b) have established endosulfan doses for acute dietary exposure as 15 ng g^{-1} day^{-1} and 1.5 ng g^{-1} day^{-1} for adults and children, respectively. In case of chronic dietary exposure, reference doses are 6.0 ng g^{-1}d^{-1} for adults and 0.06 ng g^{-1} day^{-1} in children. However, other international organizations such as the *Canadian Council of Ministers of the Environment* have no guidelines on the quantity of endosulfan residues in tissues of aquatic biota that is safe for consumers (CCME, 2014). The same situation occurs in Mexico, where there is no legislation providing permissible concentrations of pesticides such as endosulfan and its isomers; the official standard NOM-242-SSA1-2009 (Diario Oficial, 2011), which specifically deals with commercially important aquatic organisms and is also responsible for regulating the conditions for fishery products (fresh, chilled, frozen or processed), does not consider such contaminants in its content.

For occupational exposure, the National Institute for Occupational Safety and Health recommended a limit of 100 ng g^{-1} for endosulfan in air as an average over a period of 10 hours (NIOSH, 2011). An acceptable level of exposure of operators to endosulfan (AOEL) is a concentration of 0.0042 mg kg^{-1} day^{-1} (CE, 2005). However, the Administration of Occupational Safety and Health (OSHA) has not set a legal limit for endosulfan in the air for a period of 8 hours (ATSDR, 2013).

The reference values for α and β endosulfan for the protection of freshwater aquatic life indicate that the acute and chronic effects are reported at concentrations between 220,000,000 and 56,000,000 ng L^{-1}, respectively. As for marine organisms, acute effects exist at 34,000,000 ng L^{-1} and chronic effects begin at concentrations of 8,700,000 ng L^{-1} (EPA, 2014). A criterion for total endosulfan was established for protection of aquatic life in freshwater and seawater, where levels of 60 ng L^{-1} for acute exposure and 3.0 ng L^{-1} for chronic exposure were established for freshwater. For seawater, the values fluctuated between 90 and 2.0 ng L^{-1} for the acute and chronic exposure, respectively (CCME, 2014). As a result of comparing the various permissible limits stipulated by different international agencies, some discrepancies were found in the reference values established and the considerations that governed them. Therefore, the permissible limits for endosulfan application represent an important way to protect public health and the environment, particularly for food intake by aquatic organisms, which have been shown to contain contaminants such as endosulfan (Table 3).

Table 3. Regulation of endosulfan exposure dose based on exposure route

Exposure route	Specifying criteria	Permissible limits	Reference
Food	Assessment of exposure risk	Acceptable Daily Intake (ADI) of 6 ng g^{-1} day^{-1}	CE (2005)
		Reference dose for acute oral exposure (RfD): 15 ng g^{-1} day^{-1}	
	Total diet studies	Acceptable Daily Intake (ADI) of 6 ng g^{-1} day^{-1}	WHO (2005)
	Acute dietary exposure to endosulfan	Adults, 15 ng g^{-1} day^{-1}	EPA (2002b)
		Children, 1.5 ng g^{-1} day^{-1}	
	Chronic dietary exposure to endosulfan	Adults, 6.0 ng g^{-1} day^{-1}	
		Children, 0.06 ng g^{-1} day^{-1}	
	Public health for endosulfan (α, β) and endosulfan sulfate	Endosulfan sulfate in lakes, rivers, streams plus organisms, 62,000 ng L^{-1}	EPA (2009)
	Public health for endosulfan (α, β) and endosulfan sulfate	A limit of 89,000 ng L^{-1} was established in body organism only.	
	Fishery products (fresh, chilled, frozen and processed)	Not legislated	Diario Oficial (2011)
Occupational	National Institute of Health and Occupational Safety (NIOSH)	1×10^{5} ng m^3 in the air, as an average 10 hours day^{-1}	NIOSH (2011)
	Acceptable level of exposure for operators (AOEL)	4.2 ng g^{-1} day^{-1}	CE (2005)
Aquatic life	Protection of aquatic life in fresh and marine waters	Freshwater: acute effects, 60 ng L^{-1}	CCME (2014)
		Chronic effects, 3.0 ng L^{-1}	
		Freshwater: acute effects, 90 ng L^{-1}	
		Chronic effects, 2.0 ng L^{-1}	
	Protection of aquatic life in fresh and marine water against endosulfan α and β	Freshwater acute effects, 220,000,000 ng L^{-1}	EPA (2014)
		Chronic effects, 56,000,000 ng L^{-1}	
		Marine water acute effects, 34,000,000 ng L^{-1}	
		Chronic effects, 8,700,000 ng L^{-1}	
	Protection of freshwater aquatic life	Chronic exposure, 56 ng L^{-1}	EPA (2002)

7. Use of Endosulfan in Mexico

When identifying patterns of pesticide use along the Gulf of Mexico coast, a total application volume of endosulfan was reported as an active ingredient with 41,755 kg for the geographic units analyzed. Areas with the highest application volume were those for the Pánuco River with 33,826 kg, followed by Tuxpan, Cazones and

Tecolutla rivers with 2,363 kg. Moreover, this pesticide represented 40% of the 41 compounds used in the area and ranked second in having a high relative value of environmental risk due to the large volumes used, toxicity and persistence (Benítez & Barcenas, 1996).

In Mexico, there is a lack of public information on the volume of pesticides applied, including endosulfan, which is authorized for 41 crops (Bejarano et al., 2008, 2009). An increase in the importation of this compound has been reported, from 119 t in 2002 to 731 t in 2006. There also is a total lack of public access to information on this chemical, such as where and how much was used, the extent of authorized permissions, their intrinsic characteristics as POPs, as well as the environmental dispersion to aquatic ecosystems (Rendón & Bejarano, 2010).

Endosulfan, as reported by the Federal Commission for the Protection against Sanitary Risk (COFEPRIS-abbreviation by initials of a Mexican institution) in December 2008, had 85 authorized permissions for its agricultural use as an active ingredient, while as a formulated product it included 20 crops, such as vegetables, gramineous, legumes and fruits (Rendón & Bejarano, 2010). This agrees with reports indicating that in Mexico, the use of endosulfan as an insecticide is authorized for more than 20 crops (RAPAM, 2014). Due to the extensive use of the compound, nearly 4,000 t were imported for its formulation during the period from 2002 to 2010, with the primary sources being Germany, India and Israel (Rendón & Bejarano, 2010; RAPAM, 2014).

COFREPIS, through consultation on the commercial registering of authorized pesticides, indicates that endosulfan, as an active ingredient, has 35 records, which correspond to various trade companies, but whose validity is undetermined (COFREPIS, 2014). Therefore, it is important to know the historical trends of pesticides such as endosulfanin order to estimate dietary intake of various foods and to identify their origins to help ensure food safety for consumers (Desalegn et al., 2011).

The imports of endosulfan into Mexico in 2006 exceeded 640 t, representing the highest volume ever traded. Fluctuations in the imported volume of this pesticide over the past 10 years exist, with 303 and 504 t in 2009 and 2010, respectively (INE, 2011). According to the Tariff Information System via Internet (SIAVI), the same trend was evident where 435.55 t were imported in 2012, and by 2013 it had decreased to only 60 t (SIAVI, 2014). However, despite the decline in imported endosulfan, according to SIAVI the presence of this compound in food products such as aquatic organisms remained alarmingly high. Thus, despite the commitment to eradicating its use, endosulfan is still used in Mexico. Also, through the consultation of various sources of information (Bejarano et al., 2008, 2009; INE, 2011; RAPAM, 2014; COFEPRIS, 2014), some discrepancy was found in the number of authorized records reported for this pesticide, which highlights the need for accurate information on how much endosulfan is used and how it is applied.

8. Presence in Aquatic Organisms

8.1 Bivalve Molluscs

The oyster *Crassostrea virginica* (Gmelin) is one of the molluscs most commonly used as a bioindicator in the Gulf of México. The species has been used as an important indicator of various persistent organic compounds, among them endosulfan, not only for its ecological significance, but also for its economical importance. However, investigations on levels of organochlorine pesticides such as endosulfan are widely scattered and scarce in some regions of Mexico.

The ecological risk of Σendosulfan in *C. virginica* and filtered water samples in Términos Lagoon was at a concentration of 0.45 pg L^{-1}, causing toxic effects such as immobility in embryos of this oyster, and a value range of 0-37 pg L^{-1} for the water (Carvalho et al., 2009b). Given the economic, ecological and social importance of oysters, *C. virginica* is a vulnerable benthic organism in the lagoon systems in the Gulf of México due to the presence of chemical contaminants such as organochlorine pesticides (Lango et al., 2013b).

In the Gulf of México, *C. virginica* is the characteristic bivalve mollusc in lagoon systems. It has been extensively studied for the presence of pesticides including endosulfan and its isomers. Given that this species filter-feeds and is benthic, it is an organism with a potential for bioaccumulation of chemical contaminants from lakes that are directly influenced by agricultural activities in the areas surrounding these lakes. Table 4 shows the concentrations of endosulfan and its isomers chronologically (by report) and by organismal group.

Table 4. Concentration of endosulfan and its isomers (ng g^{-1}) in aquatic organisms of commercial importance in the Gulf of Mexico

Coastal lagoon	Groups and species	Isomers				
		α	β	Sulfate	∑	Reference
Bivalves						
P. Viejo	*Crassostrea virginica* (Gmelin)	--	0.06	--	--	Rosales (1979)
Tampama			N.D.			
Alvarado			N.D.			
Machona			N.D.			
Carmen			0.06			
E. Tamulte			0.06			
P. Rico			N.D.			
Términos (BA)			0.4			
Términos (PV)			N.D.			
Alvarado	*C. virginica*	1.22±0.76	17.65±7.76	N.D.	--	Botello et al.
Carmen		N.D.	14.93±6.26	N.D.		(1994)
Machona		0.83±0.38	8.78±4.52	N.D.		
Palizada River	*C. virginica*	--	--	--	9.84 (BT)	Gold et al.
and					111	(1995)
Términos	*Brachidontes recurvus*				8.23	
Alvarado	*C. virginica*	1.22	17.65	N.D.	--	Díaz and Rueda
Carmen		0.83	14.93	N.D.		(1996)
Machona		N.D.	8.78	N.D.		
Términos, Campeche	*C. virginica*	0.010-0.080	0.084-0.013	0.560-0.670	0.604-0.670	Carvalho et al. (2009a)
	C.rhizophorae Guilding					
Madre	*C. virginica*	13.97±0.30	N.D.	--	--	Lango-Reynoso
Mandinga		37.27±0.00	99.48±16.21			et al. (2013a)
Mecoacán		14.89 ±1.16	N.D.			
Alvarado	*C. virginica*	1.27, d	N.D.	0.22, r	--	Palmerín et al. (2014)
	Rangia cuneata (G.B. Sowerby I)	9.10 (max), d	4.92 (max), r	22.4 (max), r		
	Rangia flexuosa (Conrad)	0.64, r	0.66, r	4.83, r		
	Polymesoda caroliniana (Bosc)	N.D., r	N.D, r	1.35, r		
Crustaceans						
Palizada River and Términos	*Litopenaeus setiferus* (L.)	--	--	--	0.94	Gold et al. (1995)
Fish						
Chetumal Bay	*Ariopsis assimilis* (Günther)	--	R: 5±8	--	--	Vidal et al. (2003)
			B: 4±5			
			N: 3±6			
			PVe: 1±3			
			PCa: 0.3±1			
Chetumal Bay	*A. assimilis*	--	26.57 (max)	--	--	Noreña et al. (2004)
Candelaria-Panlau	*Arius melanopus* Günther	10.83±16.45	2.86±7.56	31.24±74.44	--	Díaz et al.
East Candelaria, Términos	*Cichlasoma* spp.	99	35.8	49.7		(2005)
	A. melanopus	22.38	N.D	N.D		
	Both species	21.68±35.77	5.11±13.53	7.10±18.78		
Chetumal Bay	*A. assimilis*	--	--	--	21.5 (m)	Álvarez (2009)

						40.0 (max)	
						13.0 (min)	
Términos, Campeche	*Lepisosteus tropicus* Gill		<0.002	<0.003	0.026	0.026	Carvalho et al. (2009a)

Note. N.D.: Not detected; --: Not analized; P. Viejo: Pueblo Viejo; Tampama: Tampamachoco; P. Rico: Puerto Rico; BA: Boca Atasta; PV: Palizada Vieja; Max: Maximum; Min: Minimum; r: rain; d: dry; AE: both species; m: Mediana; BT: Boca de Laguna Términos; R: Ramonal; B: Bellavista; N: Nictechan; PVe: PuntaVerde; PCa: Punta Calera.

8.2 Crustaceans

Studies on the presence of endosulfan in crustaceans in the Gulf of Mexico are scarce and mainly limited to the genus *Penaeus*. The few studies that exist are mainly focused on determining the presence of endosulfan, identifying dispersion of DDT residues and their metabolites in environmental matrices. Therefore, about 90% of research along the Mexican coast lacks information about endosulfan residues in environmental systems and aquatic biota (Rendón & Bejarano, 2010).

The ecological risks of Σendosulfan in pink shrimp, *Farfantepenaeus duorarum* (Burkenroad) and samples of filtered water from Términos Lagoon were assessed, yielding toxic effects on shrimp at 0.04 pg L^{-1} and LC_{50} concentrations in water at 8 to 22 pg L^{-1} (Carvalho et al., 2009b). These results contrast with other studies where endosulfan sulfate was found in higher concentrations, followed by alpha and beta isomers, suggesting the predominance of degraded forms produced mainly during oxidation of the alfa isomer (Montes et al., 2012).

Aquatic organisms of commercial importance such as bivalves, crustaceans and fish in the Gulf of México and the Caribbean Sea had higher concentrations of beta endosulfan, followed by the alpha isomer and endosulfan sulfate, indicating recent use of the pesticide. In previous studies, a lower concentration of the ∑endosulfan was reported on crustaceans compared to that from analyzed bivalves; a difference explained by the physiological and ecological characteristics of each species. This trend can be explained on the genus *Farfantepenaeus,* mainly because of its position on the water column and capacity for movement, although it has detritophagos habits (Table 4).

8.3 Fish

Studies on the concentration of endosulfan in fish from the Gulf of Mexico and Caribbean Sea are scarce. The potential interaction between the presence of β-endosulfan and parasitization in Mayan catfish *Ariopsis assimilis* (Günther) in the Bay of Chetumal were assessed, and revealed a lack of a positive correlation between the presence of the β-isomer and the intensity of parasitic infestation (Vidal et al., 2003). The detected concentrations were lower than those reported for the same species (Noreña-Barroso et al., 2004; Álvarez, 2009).

Higher concentrations of this compound in fish can be explained as a process of biomagnification, given that these organisms feed on shrimp, crabs and small fish. The concentrations are also associated with the amount of lipids present within consumer tissues, which promotes the accumulation of organochlorine compounds such as endosulfan due to their lipophilic affinity. Thus, within fish species of commercial importance in the Gulf and Caribbean, only four were found in studies that address this pollutant. Reports indicated that through management programs such as Fisheries Management Plans (FMP), which provide insight into the impacts of production and development activities in each lagoon system, FMP strategic targets can be met for sustainable fisheries (Castañeda et al., 2014).

Analysis of endosulfan concentrations in the different organism groups show different sources of influence on the bioaccumulation of organochlorine pesticides such as endosulfan in aquatic organisms: feeding habits, position in the water column (ecological habits) and the incorporation of these pollutants, either through water or sediment, which can promote progressive bioaccumulation.

8.4 Strategies for Endosulfan Reduction Use

Certainly, endosulfan is an organochloride pesticide that affects the aquatic life in the Gulf of México and collaterally has an impact on public health, which is a concern that should be seriously taken in account by many actors in the society, especially with the aid of government-funded programs. In this case, the short and long-term strategy proposed by Galavis-Villa et al. (2010) to reduce water contamination by nitrate and nitrite could be applied to reduce endosulfan contamination in different environments. In the short-term workshops can be implemented to teach people not only about the danger of using endosulfan and the implicated risks but

inform them of the different/reduction options available, and to train them when using it. As a long-term strategy it is important to reduce the use of the pesticide by optimizing timing and rates based on a protective program. These strategies to reduce the negative impacts on the environment and public health can be implemented at municipality level in developing countries. In other cases or situations, such strategies can be accomplished at smaller scales depending on the educational and economical levels of the society under consideration.

9. Conclusions

The presence of endosulfan and its isomers indicates the need to increase the number of studies of its effect on water quality and pollution of shellfish and fish for human consumption due to the various adverse effects reported on public health. Moreover, there are large gaps in information because of the lack of continuity in monitoring programs. Therefore, it is necessary to identify the exact sources of emission of these compounds, to know how they are mobilized toward coastal lagoons, and to understand their effects on wildlife (plant and animal, aquatic and terrestrial) in these ecosystems. Efficient screening mechanisms should also be employed to reduce exposure to endosulfan in consumer products such as aquatic organisms. Finally, it is necessary to have more strict national laws to ensure that the consumption of aquatic organisms is free of toxic compounds such as endosulfan.

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References

Albert, L. A. (2014). Los plaguicidas y sus riesgos para el ambiente. In A. V. Botello, J. Rendón von Osten, J. Benítez, & G. Gold-Bouchot (Eds.), *Golfo de México. Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (3rd ed., pp. 183-212). México D. F.: UAC, UNAM-ICMYL, CINVESTAV-Unidad Mérida.

Albert, L. A., & Benítez, J. A. (1996). Impacto ambiental de los plaguicidas en los ecosistemas costeros, In A. V. Botello, J. L. Rojas-Galaviz, J. A. Benítez, & D. Zárate-Lomelí (Eds.), *Golfo de México. Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (pp. 107-123). México D. F.: EPOMEX, Universidad de Campeche.

Alegría, H., Wong, F., Bidleman, T., Figueroa, M. S., Gold-Bouchot, G., Waliszewski, S., … Infanzon, R. (2005). Ambient air levels of organochlorine pesticides in air in southern México. In A. V. Botello, J. Rendón-von Osten, G. Gold-Bouchot, & C. Agraz-Hernández (Eds.), *Golfo de México. Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (2nd ed., pp. 225-236). México D. F.: Univ. Autónoma de Campeche, Univ. Nal. Autónoma de México, Instituto Nacional de Ecología.

Álvarez, L. T. (2009). Contaminación acuática. In J. Á. Espinoza, G. I. Alexander & H. A. Hernández-Arana (Eds.), *El Sistema Ecológico de la Bahía de Chetumal/Corozal: Costa Occidental del Mar Caribe* (pp. 205-216). México D. F.: ECOSUR.

Aly, H. A. A., & Khafagy, R. M. (2014). Taurine reverses endosulfan-induced oxidative stress and apoptosis in adult rat testis. *Food and Chemical Toxicology, 64*, 1-9. http://dx.doi.org/10.1016/j.fct.2013.11.007

ATSDR. (2000). *Toxicological Profile for Endosulfan* (p. 284). Agency for Toxic Substances and Disease Registry; U.S. Department of Health and Human Services, Public Health Service, Division of Toxicology/Toxicology Information Branch. Atlanta, GA.

ATSDR. (2001). *Reseña Toxicológica del Endosulfán* (p. 2). Agencia para Sustancias Tóxicas y el Registro de Enfermedades. Departamento de Salud y Servicios Humanos de los EE.UU. Servicio de Salud Pública. Atlanta, GA.

ATSDR. (2013). *Reseña Toxicológica del Endosulfán* (p. 2). Agencia para Sustancias Tóxicas y el Registro de Enfermedades. Departamento de Salud y Servicios Humanos de los EE.UU. Servicio de Salud Pública. Atlanta, GA.

Bajpayee M., Pandey, A. K., Zaidi, S., Musarrat, J., Parmar, D., Mathur, N., ... Dhawan, A. (2006). DNA damage and mutagenicity induced by endosulfan and its metabolites. *Environmental and Molecular Mutagenesis, 47*(9), 682-692. http://dx.doi.org/10.1002/em.20255

Bauer, M., Greenwood, S. J., Clark, K. F., Jackman, P., & Fairchild, W. (2013). Analysis of gene expression in *Homarus americanus* larvae exposed to sublethal concentrations of endosulfan during metamorphosis. *Comparatve Biochemistry and Physiology, Part D, 8*, 300-308. http://dx.doi.org/10.1016/j.cbd.2013.07.002

Bejarano, G. F. (2008). El endosulfán una amenaza a la salud y el medio ambiente. In F. Bejarano-González, J. Souza-Casadinho, J. M. Weber, C. Guadarrama-Zugastu, E. Escamilla-Prado, B. Beristáin-Ruiz, ... F. Ramírez-Muñoz (Eds.), *El Endosulfán y sus Alternativas en América Latina* (pp. 9-34). México D. F.: IPEN, RAP-ALRAPAM, UACH.

Bejarano, G. F. (2009). El endosulfán una amenaza a la salud y el medio ambiente. In F. Bejarano-González, J. Souza-Casadinho, J. M. Weber, C. Guadarrama-Zugastu, E. Escamilla-Prado, B. Beristáin-Ruiz, ... M. E. Rozas. (Eds.), *El Endosulfán y sus Alternativas en América Latina* (pp. 5-11). México D. F.: IPEN, RAP-ALRAPAM, UACH.

Benítez, J. A., & Bárcenas, C. (1996). Patrones de uso de los plaguicidas en la zona costera del Golfo de México. In A. V. Botello, J. L. Rojas-Galaviz, J. A. Benítez, & D. Zárate-Lomelí (Eds.), *Golfo de México, Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (pp. 155-167). México D. F.: EPOMEX. Universidad Autónoma de Campeche.

Botello, V. A., Díaz, G., Rueda, L., & Villanueva, F. S. (1994). Organochlorine compounds in oysters and sediments from coastal lagoons of the Gulf of Mexico. *Bulletin of Environmental Contamination and Toxicology, 53*, 238-245. http://dx.doi.org/10.1007/BF00192039

Carvalho, F. P., Villeneuve, J. P., Cattini, C., Rendón, J., & Mota, de O. J. (2009a). Pesticide and PCB residues in the aquatic ecosystems of Laguna de Términos, a protected area of the coast of Campeche, México. *Chemosphere, 74*, 988-995. http://dx.doi.org/10.1016/j.chemosphere.2008.09.092

Carvalho, F. P., Villeneuve, J. P., Cattini, C., Rendón, J., & Mota, de O. J. (2009b). Ecological risk assessment of PCBs and other organic contaminant residues in Laguna de Términos, México. *Ecotoxicology, 18*, 403-416. http://dx.doi.org/10.1007/s10646-008-0295-9

CCME (Canadian Council of Ministers of the Environment). (2014). *Canadian Environmental Quality Guidelines Summary Table*. Water Quality Guidelines for the Protection of Aquatic Life. Retrieved April 13, 2014, from http://ceqg-rcqe.ccme.ca

Castañeda-Chávez, M. R., Lango-Reynoso, F., Galavíz-Villa, I., & Carrillo-Alejandro, P. (2014). Diagnóstico ambiental para la formulación de un Plan de Manejo Pesquero. In A. V. Botello, J. Rendón von Osten, J. Benítez, & G. Gold-Bouchot (Eds.), *Golfo de México. Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (3rd ed., pp. 975-997). México D. F.: UAC, UNAM-ICMYL, CINVESTAV-Unidad Mérida.

CE (Comisión Europea). (2005). *Review Report for the active substance Endosulfan SANCO/4327/2000-rev. 2 Final*. February 15, 2005.

Ciglasch, H., Busche, J., Amelung, W., Totrakool, S., & Kaupenjohann, M. (2008). Field aging of insecticides after repeated application to a northern Thailand ultisol. *Journal of Agricultural and Food Chemistry, 56*(20), 9555-9562. http://dx.doi.org/10.1021/jf801545h

COFREPIS (Comisión Federal para la Protección contra Riesgos Sanitarios). (2014). *Registro de plaguicidas: Endosulfán*. Retrieved November, 19, 2014 from http://189.254.115.250/Resoluciones/Consultas/ConWebR egPlaguicida.asp

Desalegn, B., Takasuga, T., Harada, K. H., Hitomi, T., Fujii, Y., Yang, H. R., ... Koizumi, A. (2011). Historical trends in human dietary intakes of endosulfan and toxaphene in China, Korea and Japan. *Chemosphere, 83*, 1398-1405. http://dx.doi.org/10.1016/j.chemosphere.2011.02.063

Diario Oficial. (2011). NOM-242-SSA1-2009. *Norma oficial Mexicana NOM-242-SSA1-2009, Productos y servicios. Productos de la pesca frescos, refrigerados, congelados y procesados. Especificaciones sanitarias y métodos de prueba* (p. 128). Secretaría de Salud, 10 de Febrero de 2011. México D. F.: Diario Oficial de la Federación.

Díaz, G., & Rueda, Q. N. L. (1996). Niveles de concentración de plaguicidas organoclorados en las lagunas del Carmen, Machona y Alvarado. In A. V. Botello, J. L. Rojas-Galaviz, J. A. Benítez, & D. Zárate-Lomelí (Eds.), *Golfo de México, Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (pp. 177-185). México D. F.: EPOMEX. Universidad Autónoma de Campeche.

Díaz, G., Botello, A. V., & Ponce-Vélez, G. (2005). Plaguicidas organoclorados en pastos y peces de los sistemas Candelaria-Panlau y Palizada del Este, Laguna de Términos, Campeche, México. In A. V. Botello, J. Rendón-von Osten, G. Gold-Bouchot, & C. Agraz-Hernández (Eds.), *Golfo de México. Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (2nd ed., pp. 207-224). México D. F.: Univ. Autónoma de Campeche, Univ. Nal. Autónoma de México, Instituto Nacional de Ecología.

EPA. (2002). *National Recommended Water Quality Criteria: 2002*. Bulletin from the Office of Science and Technology, Division of Health and Ecological Criteria. U.S. Environmental Protection Agency, Washington, DC. Retrieved November 21, 2014, from http://water.epa.gov/scitech/swguidance/standards/upload/2008_04_29_criteria_wqctable_nrwqc-2002.pdf

EPA. (2002b). *Registration eligibility decision for endosulfan*. United States Environmental Protection Agency, Washington D.C. Retrieved October 27, 2014 from http://www.epa.gov/oppsrrd1/REDs/endosulfan_red.pdf

EPA. (2009). *National recommended water quality criteria*. Washington, D.C.: Office of Water, Office of Science and Technology, U.S. Environmental Protection Agency. Retrieved September 16, 2014, from http://water.epa.gov/scitech/swguidance/standards/criteria/current/upload/nrwqc-2009.pdf

EPA. (2014). *National Recommended Water Quality Criteria, Aquatic Life Criteria Table: Alpha + beta endosulfan*. Retrieved October 10, 2014, from http://water.epa.gov/scitech/swguidance/standards/criteria/current/index.cfm#organoleptic

FAO. (2000). *Evaluación de la contaminación en suelo. Manual de referencia*. Colección 8: Eliminación de los plaguicidas. Roma, Italia. Retrieved from http://www.fao.org/docrep/005/x2570s/X2570S02.htm

Galaviz-Villa, I., Landeros-Sánchez., C., Castañeda-Chávez, M. R., Martínez-Dávila, J. P., Pérez-Vázquez, A., Nikolskii-Gavrilov, I., & Lango-Reynoso, F. (2010). Agricultural contamination of subterranean water with nitrates and nitrites: an environmental and public health problema. *Journal of Agricultural Science, 2*(2), 17-30. http://dx.doi.org/10.5539/jas.v2n2p17

Gioia, R., Offenberg, J. H., Gigliotti, C. L., Totten, L. A., Du, S., & Eisenreich, S. J. (2005). Atmospheric concentrations and deposition of organochlorine pesticides in the U.S. mid-Atlantic region. *Atmospheric Environment, 39*, 2309-2322. http://dx.doi.org/10.1016/j.atmosenv.2004.12.028

Gold, B. G., Silva, H. T., & Zapata, P. O. (1995). Organochlorine pesticide residue concentrations in biota and sediments from Rio Palizada, Mexico. *Bulletin of Environmental Contamination and Toxicology, 54*, 554-561.

Haffmans, S., Bejarano, F., Davo-Vodouhe, S., Watts, M., Weber, C., & Williamson, S. (2008). *Introducir gradualmente alternativas del endosulfán* (p. 7). PAN Germany. PAN International. Hamburg, Germany.

Hageman, K. J., Simonich S. L., Campbell, D. H., Wilson, G. R, & Landers, D. H. (2006). Atmopsheric deposition of current-use and historic-use pesticides in snow at national parks in the western United States. *Environmental Science & Technology, 40*, 3174-3180. http://dx.doi.org/10.1021/es060157c

Hapeman, C. J., McConnell, L. L., Potter, T. L., Harman, F. J., Schmidt, W. F., Rice, C. P., ... Curry, R. (2013). Endosulfan in the atmosphere of South Florida: Transport to Everglades and Biscayne National Parks. *Atmospheric Environment, 66*, 131-140. http://dx.doi.org/10.1016/j.atmosenv.2012.04.010

Hose, G. C., Lim, R. P., & Hyne, R. V. (2003). The transport, fate and effects of endosulfan in the Australian freshwater environment. *Australasian Journal of Ecotoxicology, 9*, 101-111.

INE (Instituto Nacional de Ecología). (2011). *Diagnóstico de la situación del endosulfán en México* (p. 48). Secretaría de Medio Ambiente y Recursos Naturales(SEMARNAT). México D. F.

INECC (Instituto Nacional de Ecología y Cambio Climático). (2014). *Fichas técnicas de los herbicidas incluidos en el catálogo CICOPLAFEST 2004: Endosulfán*. Retrieved October 12, 2014 from http://www2.inecc.gob.mx/sistemas/plaguicidas/pdf/endosulfan.pdf

INIA. (1999). *Monograph prepared in the context of the inclusion of the following active substance in Annex I of the Council Directive 91/414/EEC* (p. 159). Instituto Nacional de Investigación y Tecnología Agraria y Alimentaria (I.N.I.A.). Madrid, Spain.

IPEN. (2005). Endosulfán. Respuesta a preguntas frecuentes. Argumentos de prohibición mundial. *International POPs Elimination Network* (1st ed., p. 28). Kerela, India: THANAL.RAPAL.RAPAM.

Jones, W. (2002). *Degradation of [14C] Endosulfan in two aerobic water/sediment systems*. Reference: C022921. EU. Additional Information Dossier.

Jones, W. (2003). *Degradation of [14C] Endosulfan in two aerobic water/sediment systems (under acid conditions)*. Reference: C031060. EU Additional Information Dossier.

Kidd, H., & James, D. R. (1991). *The Agrochemicals Handbook* (3rd ed., pp. 5-14). The Royal Society of Chemistry, Cambridge, UK.

Lango-Reynoso, F., Castañeda-Chávez, M. R., Landeros-Sánchez, C., Galavíz-Villa, I., Navarrete-Rodríguez, G., & Soto-Estrada, A. (2013a). Cd, Cu, Hg and Pb, and organochlorine pesticides in commercially important benthic organisms from coastal lagoons along the SW Gulf of Mexico. *Agricultural Science, 1*, 63-80. http://dx.doi.org/10.12735/as.v1i1p63

Lango, R. F., Castañeda, C. M. R., & Navarrete, R. G. (2013b). Perfil de contaminantes del ostión Crassostrea virginica en el Golfo de México. In D. Aldana, M. Enriqúez, & V. Elías (Eds.), *Manejo de los recursos pesqueros de la cuenca del Golfo de México y del Mar Caribe* (pp. 87-113). México D. F.: La ciencia en Veracruz.

Li, Y. F., & Li, D. C. (2004). *Global emission inventories for selected organochlorine pesticides*. Internal Report, Meteorogical Service of Canada. Toronto, Canada, 7 Environment Canada.

Li, Y. F., & Macdonald, R. W. (2005). Sources and pathways of selected organochlorine pesticides to the Arctic and the effect of pathway divergence on HCH trends in biota: A review. *Science of the Total Environment, 342*, 87-106. http://dx.doi.org/10.1016/j.scitotenv.2004.12.027

Maier-Bode, H. (1968). Properties, effect, residues and analytics of the insecticide endosulfan. *Residue Reviews, 22*, 1-44. http://dx.doi.org/10.1007/978-1-4615-8434-6_1

Mobarak, Y. M., & Al-Asmari, M. A. (2011). Endosulfan impacts on the developing chick embryos: morphological, morphometric and skeletal changes. *International Journal of Zoological Research, 7*(2), 107-127. http://dx.doi.org/10.3923/ijzr.2011.107.127

Montes, A. M., González-Farias, F. A., & Botello, V. A. (2012). Pollution by organochlorine pesticides in Navachiste-Macapule, Sinaloa, Mexico. *Environmental Monitoring and Assessment, 184*(3), 1359-1369. http://dx.doi.org/10.1007/s10661-011-2046-2

Nandar, K. S., Gopel, T. A., Pal, S. K., Kumar, A., Afroz., J. M., & Damu, P. R. (2011). Experimentally induced toxicity of ocharatoxin A and endosulfan in male wistar rats: a hormonal disorder. *Journal of Animal and Veterinary Advances, 10*(13), 1750-1755. http://dx.doi.org/10.3923/javaa.2011.1750.1755

Negro, C. L., Castiglioni, M., Senkman, L. E., Loreste, A., & Collins, P. (2013). Costo of reproduction. Changes in metabolism and endosulfán lethality caused by reproductive behavior in Hyalella curvispina (Crustacea: Amphipoda). *Ecotoxicology and Environmental Safety, 90*, 121-127. http://dx.doi.org/10.1016/j.ecoenv.2012.12.022

Nieto, Z. O. (2001). Endosulfán. In Organización Panamericana de la Salud, *Fichas técnicas de plaguicidas a prohibir o restringir incluídos en el acuerdo No. 9 de la XVI Reunión del Sector Salud de Centroamérica y República Dominicana (RESSCAD). Documento 13777* (pp. 146-147). San José, Costa Rica.: Organización Panamericana de la Salud. Organización Mundial de la Salud. Programa Medio Ambiente y Salud en el Istmo Centroamericano.

NIOSH. (2011). *Endosulfan. NIOSH pocket guide to chemical hazards*. Atlanta, GA: National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention. Retrieved November 18, 2014, from http://www.cdc.gov/niosh/npg

Noreña-Barroso, E., Simá-Álvarez, R., Gold-Bouchot, G., & Zapata-Pérez, O. (2004). Persistent organic pollutants and histological lesions in Mayan catfish *Ariopsis assimilis* from the Bay of Chetumal, Mexico. *Marine Pollution Bulletin, 48*, 263-269. http://dx.doi.org/10.1016/j.marpolbul.2003.08.001

Palmerín, R. C., Ponce, V. G., & Botello, A. V. (2014). Evaluación de plaguicidas organoclorados en sedimentos y organismos filtradores de la laguna de Alvarado, Veracruz, México. In A. V. Botello, J. Rendón von Osten, J. Benítez, & G. Gold-Bouchot (Eds.), *Golfo de México. Contaminación e Impacto Ambiental: Diagnóstico y Tendencias* (3rd ed., pp. 285-308). México D. F.: UAC, UNAM-ICMYL, CINVESTAV-Unidad Mérida.

PANAP. (2009). Endosulfan. *Pesticide Action Network Asia & Pacific* (2nd ed.). Retrieved September 29, 2014, from http://www.pan-germany.org/download/Endo_09_PANAP_monograph_2nd%20Edition

Potter, T. L., Hapeman, C. J., McConnell, L. L., Harman-Fetcho, J. A., Schmidt, W. F., Rice, C. P., & Schaffer, B. (2014). Endosulfan wet deposition in Southern Florida (USA). *Science of the Total Environment, 468-469*, 505-513. http://dx.doi.org/10.1016/j.scitotenv.2013.08.070

Pro-Agro. (2014a). *Meteoro 35 ce. Pro-Agro*. Retrieved October 8, 2014, from. http://www.pro-agro.com.mx/prods/cheminova/cheminova23.htm

Pro-Agro. (2014b). *Thiodan® 35 ce. Pro-Agro*. Retrieved October 8, 2014, from

http://www.pro-agro.com.mx/prods/bayer/bayer81.htm

RAPAM (Red de Acción en Plaguicidas y sus Alternativas en México). (2014). *Endosulfán*. RAPAM/CAATA. Retrieved October 12, 2014, from http://www.rapam.org/endosulfn.html

Rastogi, D., Narayan, R., Saxena, D. K., & Chowdhuri, D. K. (2014). Endosulfan induced cell death in Sertoli-germ cells of male Wistar rat follows intrinsic mode of cell death. *Chemosphere, 94*, 104-115. http://dx.doi.org/10.1016/j.chemosphere.2013.09.029

Rendón von Osten, J., & Bejarano, F. (2010). Residuos de endosulfan en ecosistemas acuáticos de México. *Revista Jaina, 21*(2), 41-46.

Rosales, M. T. L., Botello, V. A., Bravo, H., & Mandelli, E. F. (1979). PCBs and organochlorine insecticides in oysters from coastal lagoons of the Gulf of Mexico, Mexico. *Bulletin of Environmental Contamination and Toxicology, 21*, 652-656. http://dx.doi.org/10.1007/BF01685484

Saiyed, H., Dewan, A., Bhatnagar, V., Shenoy, U., Shenoy, R., Rajmohan, H., ... Lakkad, B. (2003). Effect of endosulfan on male reproductive development. *Environmental Health Perspectives, 111*(16), 1958-1962. http://dx.doi.org/10.1289/ehp.6271

Schmidt, W. F., Hapeman, C. J., McConell, L. L., Mookherji, S., Rice, C. P., Nguyen, J. K., ... Kim, M. S. (2014). Temperature-dependent Raman Spectroscopic evidence of and molecular-mechanism for irreversible isomerization of β-endosulfan to α-endosulfan. *Journal of Agricultural and Food Chemistry, 62*, 2023-2030. http://dx.doi.org/10.1021/jf404404w

Scremin, O. U., Chialvo, D. R., Lavarello, S., Berra, H. H., & Lucero, M. A. (2011). The environmental pollutant endosulfan disrupts cerebral cortical function at low doses. *NeuroToxicology, 32*, 31-37. http://dx.doi.org/10.1016/j.neuro.2010.12.001

SIAVI (Sistema de Información Arancelaria Vía Internet). (2014). *Estadísticas anuales del 6,7,8,9,10,10-Hexacloro-1,5,5a,6,9,9a-hexahidro-6,9-metano-2,4,3-benzodioxatiepin-3-oxido (Endosulfán) Fracción arancelaria 29209003*. Sistema de Información Arancelaria Vía Internet. Retrieved March 5, 2014, from http://200.77.231.38

Silva, M. H., & Beauvais, S. L. (2010). Human health assessment of endosulfan, I: Toxicology and hazard identification. *Regulatory Toxicology and Pharmacology, 56*, 4-17. http://dx.doi.org/10.1016/j.yrtph.2009.08.013

Silva, M. H., & Carr-Jr, W. C. (2010). Human health risk assessment of endosulfan, II: Dietary exposure assessment. *Regulatory Toxicology and Pharmacology, 56*(1), 18-27. http://dx.doi.org/10.1016/j.yrtph.2009.08.015

Silva, M. H., & Gammon, D. (2009). An assessment of the developmental, reproductive, and neurotoxicity of endosulfan. *Birth Defects Research B Developmental and Reproductive Toxicology, 86*(1), 1-28. http://dx.doi.org/10.1002/bdrb.20183

Singh, N. D., Sharma, A. K., Dwivedi, P., Patil, R. D., & Kumar, M. (2007). Citrinin and endosulfan induced teratogenic effects in Wistar rats. *Journal of Applied Toxicology, 27*(2), 143-51. http://dx.doi.org/10.1002/jat.1185

Singh, P., Volger, B., & Gordon, E. (2014). Endosulfan. In P. Wexler (Ed.), *Encyclopedia of Toxicology* (3rd ed., pp. 341-343). Academic Press, Oxford. http://dx.doi.org/10.1016/B978-0-12-386454-3.00141-X

TecnoAgro. (2013). Endosulfan. Presente y futuro. Cultivos autorizados. *Revista TecnoAgro., 87*. Retrieved September 25, 2014, from http://tecnoagro.com.mx/no-87/endosulfán-presente-y-futuro-cultivos-autorizados-dp1

TEDX (The Endocrine Disruption Exchange, Inc.). (2015). List of Potential Endocrine Disruptors. *Endosulfan*. Retrieved June 19, 2015, from http://endocrinedisruption.org/endocrine-disruption/tedx-list-of-potential-endocrine-disruptors/chemicalsearch?sname=endosulfan&action=search&sall=1&searchfor=any&scas=&searchcats=all&.x=0&.y=0

UNEP. (2007). *Propuesta sobre el endosulfán* (p. 6). UNEP/POPS/POPRC.3/5. UNEP. Stockholm Convention. Geneva, Switzerland.

UNEP. (2008). *Propuesta sobre el endosulfán. Examen de nuevas propuestas de inclusión de productos químicos en los anexos A, B o C del Convenio: Endosulfan* (p. 6). Convenio de Estocolmo. UNEP/POPS/POPRC.4/14. PNUMA. Geneva, Switzerland.

UNEP. (2009a). *Proyecto de perfil de riesgos: Endosulfán* (p. 28). Convenio de Estocolmo sobre Contaminantes Orgánicos Persistentes. Geneva, Switzerland.

UNEP. (2009b). *Una enmienda al anexo A, aprobada por la Conferencia de las Partes en el Convenio de Estocolmo sobre Contaminantes Orgánicos Persistentes, en su quinta reunión* (Decisión SC-5.3). Retrieved September 22, 2014, from http://chm.pops.int/Portals/0/download.aspx?d=UNEP-POPS-COP-CONVTEX T-A-Amendment.Sp.pdf

UNEP. (2011). Documento de orientación para la toma de decisiones. *Endosulfán* (p. 28). Convenio de Rotterdam. FAO. PNUMA. Geneva, Switzerland.

UNEP. (2013). Documento de orientación para la toma de decisiones. *Endosulfán* (p. 60). Convenio de Estocolmo. UNEP/POPS/POPRC.9/13: PNUMA. Geneva, Switzerland.

Valipour, M. (2012). Hydro-module determination for vanaei village in Eslam Abad Gharb, Iran. *ARPN Journal of Agricultural and Biological Science, 7*(12), 968-976.

Valipour, M. (2014a). Irrigation status of Americas. *Advances in Applied Agricultural Science, 2*(12), 56-72.

Valipour, M. (2014b). Pressure on renewable water resources by irrigation to 2060. *Acta Advances in Agricultural Science, 2*(8), 23-42.

Valipour, M. (2014c). Variations of irrigated agriculture indicators in different continents from 1962 to 2011. *Advances in Water Science and Technology, 1*(1), 1-14.

Valipour, M. (2015). What is the tendency to cultivate plants for designing cropping intensity in irrigated area? *Advances in Water Science and Technology, 2*(1), 1-12.

Vidal, M. V. M., Aguirre, M. M. L., Noreña, B. E., Gold, B. G., & Caballero, P. P. I. (2003). Potential interactions between metazoan parasites of the Mayan catfish *Ariopsis assimilis* and chemical pollution in Chetumal Bay, Mexico. *Journal of Helminthology, 77*, 173-184. http://dx.doi.org/10.1079/JOH2002158

Wang, D. G., Alaee, M. X., Guo, W., & Pei, Q. W. (2014). Concentration, distribution, and human health risk assessment of endosulfan from a manufacturing facility in Huai'an, China. *Science of the Total Environment, 491*, 163-169. http://dx.doi.org/10.1016/j.scitotenv.2014.01.050

Weber, J., Halsall, C. J., Muir, D., Teixeira, C., Small, J., Solomon, K., ... Bidleman, T. (2010). Endosulfan, a global pesticide: A review of its fate in the environment and occurrence in the arctic. *Science of the Total Environmental, 408*, 2966-2984. http://dx.doi.org/10.1016/j.scitotenv.2009.10.077

WHO. (2005). *Total diet studies: A recipe for safer food*. Retrieved April 22, 2014, from http://www.who.int/foodsafety/publications/chem/recipe/en

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