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Mutagenicity–Carcinogenicity as Related to Teratogenic Activity

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Following the recent use and application of the short-term tests to detect the mutagenic activity, new assays have been developed to determine what is the extent of the existing relationship between the genetic toxicity and other pathological effects.

Mutagenicity-Carcinogenicity correlation has been studied by McCann et al (1975), Barsth et al (1980) and Kawachi et al (1980) in other former works, and this correlation was determined by them as 90 %, 76 % and 67 %, respectively. In a study carried out by Laborda and Herrera (1986) on 440 pesticides which are used in Spain, carcinogenicity data were obtained only for 65 products, 46 of them were carcinogens. These authors show the high level of risk presented by the pesticides.

Other pathological effects such as teratogenicity did not show a clear correlation with the genetic toxicity (Kalter 1971). Many attempts to correlate the mutagenic and the teratogenic activities have been frustrated by several aspects: the used protocols, the inadequately standardized test models and criteria that are very ambiguous, thus making it impossible to reach concordant results. However, Scheiner and Holden (1983) had established a relationship between the teratogenicity, the mutagenicity and the carcinogenicity based on the studies made by Rinkus and Legator (1979) and by Shepard (1980).

The present review shows, with the data of the related literature concerning the mutagenicity/teratogenicity/carcinogenicity, that exists a correlation respect these hazardous activities on 45 pesticides.

MATERIAL AND METHODS

This work is a review about the teratogenicity activity of 45 pesticides in several animal species normally used in the toxicological studies, compared with the mutagenic and carcinogenic activities of them. These data were obtained from several international sources, but none from experimental studies made in our laboratories.

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RESULTS AND DISCUSSION

The following tables show the found relationship between the teratogenic, mutagenic and carcinogenic effects of several pesticides as it had been described in the refered bibliography.

Taking into account the mutagenicity-carcinogenicity relationship studied by Laborda and Herrera (1986) and following the references of Chemical Abstracts, Biological Abstracts and IARC monographs (International Agency for Research on Cancer) of 45 pesticides that are commonly used in Spain, teratogenicity data were found in 32 chemicals, 28 of them were positive and 4 were negative. From 19 products that show positive mutagenicity and carcinogenicity (Table 2), a positive teratogenic activity is present in 14 pesticides of them, negative in 1 and no data were available for the 4 chemicals that remain. From 10 products that show negative mutagenicity and carcinogenicity (Table 1), 4 were shown as data with a positive teratogenic activity, 2 of them negative, and also no data were found available for the 4 pesticides remaining. Table 3 shows the teratogenic activity of the pesticides that have positive mutagenicity and negative carcinogenicity; from 16 pesticides that were found in our review, 5 of them did not have available data, 10 of them show positive teratogenicity and only 1 shows a negative teratogenic activity. This remark could be thought as that when a chemical compound shows positive mutagenicity, there is a high risk for this compound being teratogenic, at least, in some animal species.

Table 1. Relation of the Teratogenic Activity with negative Mutagenicity and Carcinogenicity Activities

Pesticides	Teratogenic					Mutag.	Carc.
	Rat	Mouse	Hamster	Rabbit	Chi. Quail		
			Dog				
Anthraquinone		N O	D A T A				
Carbaryl	53+		46+			-	-
Chlordimeform	37-	37-	37-	37-	37-	-	-
Diazinon		N O	D A T A				
Endrin	10-	10-				-	-
Malathion	29+ 28-					-	-
Metoxychlor	28+					-	-
Naphthalene		N O	D A T A				
Nicotine		36+				-	-
Propham		N O	D A T A				

10- Dix et al 1977; 28- Khera et al 1978; 29- Kimbrough and Gaines 1968; 36- Nishimura and Nakai 1958; 37- Olson et al 1978; 46- Smalley et al 1968; 53- Weil et al 1973.

We are in agreement with Rinkus and Legator (1979) about a relationship between the mutagenicity-carcinogenicity and the teratogenic activity that obviously can exist, and for the need of more studies and detailed research works in this aspect.

Table 2. Relation of the Teratogenic Activity with positive Mutagenicity and Carcinogenicity Activities

Pesticides	Teratogenic					Mutag.	Carc.
	Rat	Mouse	Hamster Dog	Rabbit	Chi. Quail		
Acrylonitrile	34+			34+		+	+
5-Azacytidine		43+				+	+
Azinphos-Methyl		N O	D A T A				
Camphechlor	7+	24+ 25+			48+	+	+
Captan	23+	22+		33+		+	+
Cyclophosphamide	14+	6+		12+		+	+
Dichloroethane		N O	D A T A				
Dichlorvos	29+ 51+	30+		51+		+	+
Dieldrin		10+			40+	+	+
Dimethoate		5-				+	+
Epichlorydrin		N O	D A T A				
Ethylen-Thiourea	26+			26+		+	+
Heptachlor			9+	48-		+	+
Maneb	32+	2+				+	+
Nitrophen	8+	16+				+	+
Simazine		N O	D A T A				
Strobane	7+	25+	11+			+	+
Tetramine	7+ 51+					+	+
Trichlorphon	9+					+	+

2- Antonovich et al 1972; 5- Budreau and Sing 1967; 6- Chaube et al 1967; 7- Chernoff and Rogers 1976; 8- Costlow and Manson 1981; 9- Courtney and Andrews 1980; 10- Dix et al 1977; 11- Dunachie and Fletcher 1969; 12- Fritz and Hess 1971; 14- Gibson and Becker 1968; 16- Gray et al 1982; 22- Kawachi et al 1980; 23- Kennedy et al 1968; 24- Kennedy et al 1973; 25- Keplinger et al 1968; 26- Khera and Shaw 1979; 29- Kimbrough and Gaines 1968; 32- Marcon 1969; 33- McCann et al 1975; 24- Murray et al 1978; 40- Rinkus and Legator 1979; 41- Scheufer 1975; 43- Seifertova et al 1968; 48- Smith et al 1970; 51- Thorpe et al 1972.

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Table 3. Relation of the Teratogenic with positive Mutagenicity and negative Carcinogenicity Activities.

Pesticides	Teratogenic					Mutag.	Carc.
	Rat	Mouse	Hamster	Rabbit	Chi. Quail		
			Dog				
Amitrole		N O	D A T A				
B-H-C	47+			39+		+	-
Carbon Tetrachloride		N O	D A T A				
Chlordecone	7+					+	-
D.D.T.	35- 38+	52-		18-		+	-
Dicofol	4-	4+				+	-
Diphenyl	20+					+	-
Fenthion		N O	D A T A				
Lindane	39-	44+		39-		+	-
Methyl-Parathion	13+ 1-	1+				+	-
Mirex	27+	52+				+	-
Parathion	17+	50+				+	-
Quintozene		N O	D A T A				
Sodium-Arsenite	19+	19+				+	-
Tetrachlovinphos		N O	D A T A				
Zineb	45+						

1- Ackermann and Engst 1970; 4- Brown 1972; 7- Chernoff and Rogers 1976; 13- Fuchs et al 1976; 17- Harbiron 1975; 18- Hart et al 1971; 19- Hood and Bishop 1972; 20- Jensh and Brent 1972; 27- Khera et al 1976; 35- Naitein and Leibovich 1971; 38- Ottoboni 1969; 39- Palmer et al 1978; 44- Shepard 1980; 45- Shirasu 1975; 47- Shtemberg and Mametkuliev 1976; 50- Talens and Woolley 1973; 52- Ware and Good 1967.

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