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### RESEARCH ARTICLE

#### THEORETICAL PROPOSAL OF NEW MOLECULES TO REPLACE CHLORDANE

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#### Abstract

Chlordane was a most used as insecticide by farmers. Today, it is banned owing to its toxicity, bio-accumulative and persistence properties. Since then its prohibition has created more unexploited stocks in the environment. In order to still allow the use of these products, we theoretically proposed new molecules derived from it. To meet this objective, we have reduced the number of chlorine atoms in the chlordane molecule to four. Thus, the QSAR and QSPR models already established made it possible to theoretically determine  $\log LC_{50}$  and the BCF of 70 molecules proposed. The analysis of the results allowed to retain two molecules. These are (1S,2S,3R,6R,7R)-3,8,10,10-tétrachlorotricyclo[5,2,1.0<sup>2,6</sup>]dec-8-ene) and (1R,2R,3R,6R,7S)-3,8,7,8-tetrachloro-tricyclo[5.2.1.0<sup>2,6</sup>]dec-8-ene. Both molecules seem to present the best values of  $\log LC_{50}$  and BCF. In order to also verify the influence of fluorine on chlordane, we carried out another study. In this part, we have considered the two abovementioned molecules on which a substitution of four hydrogen atoms by four fluorine atoms was made. This gave the following two molecules: (1R,2S,3S,4R,6R,7S)-3,8,10,10-tetrachloro-1,4,7,9-tetrafluorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene and (1S,2S,3R,4S,6S,7S)-1,3,7,8-tetrachloro-4,9,10,10-tetrafluorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene. Both molecules show higher BCF values than the formers. This would mean that organochlorine compounds which have fluorine atoms are storable. Besides, when we consider the fact that these molecules are more absorbent, (1R,2S,3S,4R,6R,7S)-3,8,10,10-tetrachloro-1,4,7,9-tetrafluorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene and (1S,2S,3R,4S,6S,7S)-1,3,7,8-tetrachloro-4,9,10,10-tetrafluorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene appear to be less accumulable and less toxic than (1S,2S,3R,6R,7R)-3,8,10,10-tétrachlorotricyclo[5,2,1.0<sup>2,6</sup>]dec-8-ene and (1R,2R,3R,6R,7S)-3,8,7,8-tetrachloro-tricyclo[5.2.1.0<sup>2,6</sup>]dec-8-ene.

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#### Introduction:-

Organochlorine pesticides were the first synthetic pesticides used by humans to protect themselves, animals and crops. These pesticides have considerably improved the quality of life of humans from their first use in the 1930s to the 1970s [1]. But the very intense use of these pesticides has resulted in their persistence in environment due to their accumulation that depends on their lipophilicity [2]. This situation involved the prohibition of the majority of

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these pesticides. However, this prohibition generates disadvantages such as the recrudescence of malaria disease. This is why the Malaria Foundation International supports the use of DDT to fight malaria even though this use must be subject to restrictions by stating: "The consequences of the treaty will probably be better than the status quo which prevailed during the negotiations of two years ago. For the first time, there is now an insecticide whose use is restricted to the control of disease vectors, which means that the selection of resistant mosquito strains will be slower than before"[3].

In 2004, Crichton in his novel titled *State of Fear* [4] made the following declaration in favor of DDT: "Since the ban on DDT, two million of people a year, mainly children, die to malaria. This ban caused more than fifty million unnecessary deaths. Banning DDT killed more people than Hitler."

Chlordane is an organochlorine that belongs to the list of the prohibited pesticides. Its empirical formula  $C_6H_6Cl_8$  (see Figure 2) was invented for the first time in 1940 but its production on industrial scale began into 1947 in USA [5]. Its synthesis is done according to the Diels-Alder reaction proposed in Figure 1. Chlordane was used extensively in North America between 1950 and 1970 to treat crops, lawns, gardens and forests and to control termites [6]. It was also used to eliminate subterranean termites, to protect houses, gardens and for the treatment of corn, citrus fruits, vegetables and various crops [7].

But after several years of use, chlordane has been assumed to be toxic, bioaccumulative and persistent molecule that breaks down very slowly in the environment [8]. It has been detected in air [9], in water and sediment [10], in soil [11], in humans [12] and in animal tissues [13].

It can remain in the soil for more than 20 years and be transferred over long distances in the atmosphere. Chlordane has a greater impact on ovarian and uterine diseases, neurological effects, such as headache, dizziness, irritability and seizures. Chlordane is considered to be probably a carcinogen compound for human [14-16]

High concentrations of chlordane can damage the nervous system and the liver. It has been shown to have effects on the endocrine and digestive systems. It is believed to be the cause of behavioral disorders in children exposed to it before birth or during breastfeeding [6].

Its toxicity and its persistence in environment led to restriction of its use since 1983, until the prohibition of its production in 1988 by the US EPA [8]. In 1997, the UN environmental program declared chlordane as a persistent organic pollutant and in 2001 it was added to the list of the twelve major pollutants, according to the Stockholm Convention [17, 18].

With the aim to propose a series of substitute molecules for banned organochlorine pesticides, we have undertaken several studies. In this article, our objective is to propose "candidate" molecules for the substitution of chlordane. Our long-term objective is to make it possible to convert available chlordane stocks or to synthesize new molecules. These new molecules must have more interesting properties than those of the chlordane molecule. They must have the following characteristics: not very toxic, not very persistent and not very bioaccumulative.

Martins F. A, et al. [19] discussed the issue in the context of toxicity. Indeed, this team used our QSAR model established with physico-chemical descriptors and published under the title Determination of descriptors which influence the toxicity of organochlorine compounds using QSAR method [20] to predict the toxicity of fluordane, F-aldrin, F-dieldrin and pentafluorophenol (PFP) which are molecules derived respectively from chlordane, aldrin, dieldrin and pentachlorophenol (PCP). Within those molecules, the chlorine atoms have been substituted by fluorine atoms. Besides, in our case we will discuss the case of molecules obtained from chlordane but which have four chlorine atoms. The choice of four chlorine atoms is justified by the fact that the most persistent organochlorine pesticides are those which have more than four chlorine atoms in their structure. In addition to toxicity, we also discuss the case of bioconcentration factor.

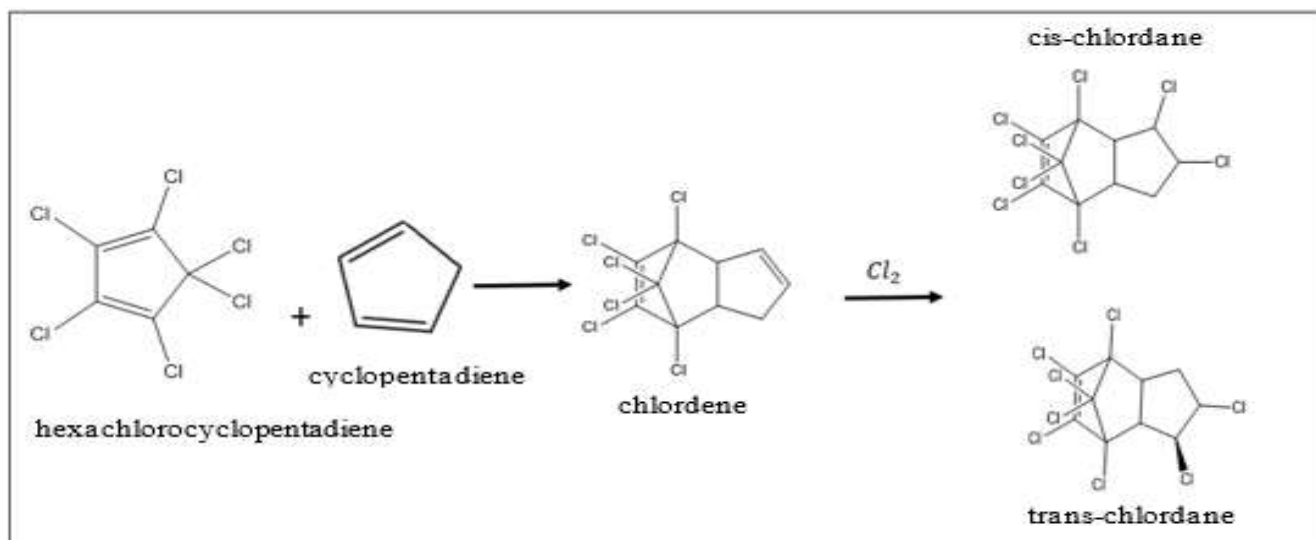


Figure 1:- Synthesis of chlordane.

### Method:-

To meet our objective, a set of molecules obtained by keeping only 4 of the 8 chlorine atoms in a chlordane molecule and replacing the remaining by hydrogen atoms was optimized. Then, with the QSAR model established in our previous article [20] and the QSPR model established in the second article [21], we theoretically determine the values of  $\log LC_{50}$  and BCF of those new molecules. Moreover, through a comparison of these values, the molecules exhibiting the best values of  $\log LC_{50}$  and / or of BCF were selected. Furthermore, we also checked the effect of fluorine on chlordane. Therefore, the four chlorine atoms which have been substituted by hydrogen atoms previously will be substituted by 4 fluorine atoms in this second part. Because, organofluorine compounds have been widely used as pesticides [22]. They are assumed to present several advantages over organochlorine compounds. In fact, these compounds have a reduced steric effect and improved electronic effects. They are more soluble compared to organochlorine compounds despite the stability of the C-F bond. The energy of the C-F bond is approximately 480 kJ/mol compared to 320 kJ/mol for the C-Cl bond. This great stability could lead to a persistence of these compounds in the environment. Yet, they are generally inert and more polar (less hydrophobic) than organochlorines, thereby suggesting less toxicity [23; 24].

The total number of molecules to be optimized according to equation below is:

$$C_8^4 = 70$$

So, 70 new geometrical isomers have been proposed. For each new molecule, we determined the logarithm of lethal concentration ( $\log LC_{50}$ ) and the bioaccumulation factor (BCF).

The values of  $\log LC_{50}$  and BCF were obtained respectively from equations (1) and (2).  $\log LC_{50} = 3.72 - 0.14 * \log P - 0.29 * \alpha + 3.17E - 02 * S - 5.70E - 04 * ZPE - 0.36 * NCl(1)$

$$BCF_{theo} = 7.35 + 7.51E - 02 * Cv - 0.70 * \%H - 5.65 * D + 0.80 * \log P \quad (2)$$

The optimization was performed with Gaussian 03 at B3LYP/6-311++g(d,p) level. The DFT method was used because this method presents the best compromise between calculation time and quality and is well suited for the study of organic compounds [25].

### Results and Discussion:-

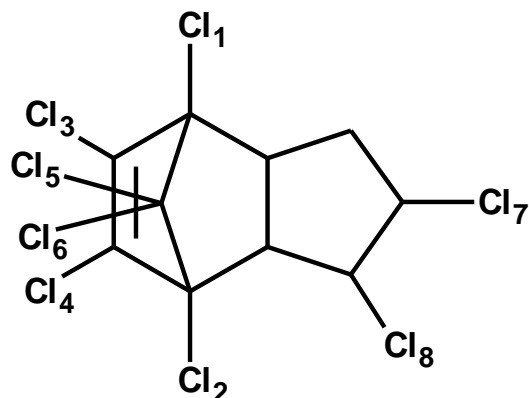
#### Analysis of Results

Table 1 shows the different molecules with the descriptors involved in the QSAR or QSPR equations, the values of  $\log LC_{50}$  and the BCF as functions of the positions of the chlorine atoms. Moreover, Figure 2 displays the structure of the chlordane with the eight chlorine atoms numbered.

N°	Index associated to molecules	Nature of atoms as a function of positions								Descriptors								<i>logLC<sub>50</sub></i>	<i>BCF</i>
		1	2	3	4	5	6	7	8	<i>logP</i>	$\alpha$	<i>S</i>	<i>ZPE</i>	<i>N<sub>Cl</sub></i>	<i>C<sub>V</sub></i>	%H	<i>d</i>		
1	Chlordane	Cl	Cl	Cl	Cl	Cl	Cl	Cl	Cl	5.57	31.82	136.53	-4066.37	8.00	63.32	1.48	1.80	<b>-2.59</b>	<b>26.32</b>
2	1234	Cl	Cl	Cl	Cl	H	H	H	H	3.94	24.17	111.77	-2227.87	4.00	48.34	3.71	1.52	<b>-0.52</b>	<b>19.11</b>
3	1235	Cl	Cl	Cl	H	Cl	H	H	H	3.94	24.25	111.26	-2227.88	4.00	48.86	3.71	1.51	<b>-0.56</b>	<b>19.27</b>
4	1236	Cl	Cl	Cl	H	H	Cl	H	H	3.94	24.25	111.22	-2227.87	4.00	48.50	3.71	1.51	<b>-0.56</b>	<b>19.24</b>
5	1237	Cl	Cl	Cl	H	H	H	Cl	H	3.27	24.25	111.55	-2227.88	4.00	48.20	3.71	1.51	<b>-0.45</b>	<b>19.22</b>
6	1238	Cl	Cl	Cl	H	H	H	H	Cl	3.13	24.25	112.18	-2227.89	4.00	48.63	3.71	1.51	<b>-0.41</b>	<b>19.25</b>
7	1245	Cl	Cl	H	Cl	Cl	H	H	H	3.94	24.25	111.25	-2227.88	4.00	48.86	3.71	1.51	<b>-0.56</b>	<b>19.27</b>
8	1246	Cl	Cl	H	Cl	H	Cl	H	H	3.94	24.25	111.39	-2227.88	4.00	48.79	3.71	1.51	<b>-0.55</b>	<b>19.26</b>
9	1247	Cl	Cl	H	Cl	H	H	Cl	H	3.27	24.25	111.85	-2227.89	4.00	48.57	3.71	1.51	<b>-0.44</b>	<b>19.25</b>
10	1248	Cl	Cl	H	Cl	H	H	H	Cl	3.17	24.25	112.34	-2227.89	4.00	48.66	3.71	1.51	<b>-0.41</b>	<b>19.25</b>
11	1256	Cl	Cl	H	H	Cl	Cl	H	H	4.13	24.35	111.77	-2227.87	4.00	48.34	3.71	1.51	<b>-0.60</b>	<b>19.31</b>
12	1257	Cl	Cl	H	H	Cl	H	Cl	H	3.37	24.33	110.50	-2227.87	4.00	48.35	3.71	1.50	<b>-0.52</b>	<b>19.35</b>
13	1258	Cl	Cl	H	H	Cl	H	H	Cl	3.34	24.33	111.59	-2227.89	4.00	48.94	3.71	1.50	<b>-0.49</b>	<b>19.39</b>
14	1267	Cl	Cl	H	H	H	Cl	Cl	H	3.37	24.33	110.88	-2227.88	4.00	48.30	3.71	1.50	<b>-0.51</b>	<b>19.35</b>
15	1268	Cl	Cl	H	H	H	Cl	H	Cl	3.34	24.33	111.10	-2227.87	4.00	48.42	3.71	1.50	<b>-0.50</b>	<b>19.35</b>
16	1278	Cl	Cl	H	H	H	H	Cl	Cl	3.02	24.33	111.05	-2227.89	4.00	48.49	3.71	1.50	<b>-0.46</b>	<b>19.36</b>
17	1345	Cl	H	Cl	Cl	Cl	H	H	H	4.36	24.15	111.95	-2227.88	4.00	48.25	3.71	1.51	<b>-0.57</b>	<b>19.14</b>
18	1346	Cl	H	Cl	Cl	H	Cl	H	H	4.36	24.15	112.01	-2227.87	4.00	47.89	3.71	1.51	<b>-0.57</b>	<b>19.11</b>
19	1347	Cl	H	Cl	Cl	H	H	Cl	H	3.90	24.15	112.24	-2227.89	4.00	47.92	3.71	1.51	<b>-0.49</b>	<b>19.12</b>
20	1348	Cl	H	Cl	Cl	H	H	H	Cl	3.95	24.15	112.39	-2227.88	4.00	47.70	3.71	1.51	<b>-0.49</b>	<b>19.10</b>
21	1356	Cl	H	Cl	H	Cl	Cl	H	H	4.16	24.25	110.63	-2227.86	4.00	48.99	3.71	1.51	<b>-0.61</b>	<b>19.28</b>
22	1357	Cl	H	Cl	H	Cl	H	Cl	H	3.61	24.23	111.45	-2227.89	4.00	48.24	3.71	1.50	<b>-0.50</b>	<b>19.26</b>
23	1358	Cl	H	Cl	H	Cl	H	H	Cl	3.73	24.23	111.50	-2227.87	4.00	48.01	3.71	1.50	<b>-0.51</b>	<b>19.24</b>
24	1367	Cl	H	Cl	H	H	Cl	Cl	H	3.73	24.23	112.03	-2227.87	4.00	47.89	3.71	1.50	<b>-0.50</b>	<b>19.23</b>
25	1368	Cl	H	Cl	H	H	Cl	H	Cl	3.73	24.23	113.04	-2227.86	4.00	46.26	3.71	1.50	<b>-0.47</b>	<b>19.11</b>
26	1378	Cl	H	Cl	H	H	H	Cl	Cl	3.63	24.23	111.25	-2227.88	4.00	47.50	3.71	1.50	<b>-0.51</b>	<b>19.21</b>
27	1456	Cl	H	H	Cl	Cl	Cl	H	H	4.12	24.25	110.74	-2227.86	4.00	48.77	3.71	1.51	<b>-0.60</b>	<b>19.26</b>
28	1457	Cl	H	H	Cl	Cl	H	Cl	H	3.57	24.23	111.88	-2227.88	4.00	47.75	3.71	1.50	<b>-0.48</b>	<b>19.22</b>
29	1458	Cl	H	H	Cl	Cl	H	H	Cl	3.72	24.23	112.06	-2227.87	4.00	48.12	3.71	1.50	<b>-0.50</b>	<b>19.25</b>
30	1467	Cl	H	H	Cl	H	Cl	Cl	H	3.57	24.23	111.83	-2227.87	4.00	47.96	3.71	1.50	<b>-0.48</b>	<b>19.24</b>
31	1468	Cl	H	H	Cl	H	Cl	H	Cl	3.72	24.23	112.92	-2227.89	4.00	48.32	3.71	1.50	<b>-0.47</b>	<b>19.27</b>
32	1478	Cl	H	H	Cl	H	H	Cl	Cl	3.62	24.23	111.79	-2227.88	4.00	47.64	3.71	1.50	<b>-0.49</b>	<b>19.22</b>
33	1567	Cl	H	H	H	Cl	Cl	Cl	H	3.48	24.33	109.88	-2227.86	4.00	48.49	3.71	1.50	<b>-0.56</b>	<b>19.36</b>
34	1568	Cl	H	H	H	Cl	Cl	H	Cl	3.70	24.33	110.23	-2227.86	4.00	48.69	3.71	1.50	<b>-0.58</b>	<b>19.37</b>

35	1578	Cl	H	H	H	Cl	H	Cl	Cl	3.51	24.31	110.44	-2227.87	4.00	47.74	3.71	1.50	<b>-0.54</b>	<b>19.29</b>
36	1678	Cl	H	H	H	H	Cl	Cl	Cl	3.51	24.31	111.29	-2227.89	4.00	48.07	3.71	1.50	<b>-0.51</b>	<b>19.31</b>
37	2345	H	Cl	Cl	Cl	Cl	H	H	H	4.36	24.15	111.96	-2227.88	4.00	48.25	3.71	1.51	<b>-0.57</b>	<b>19.14</b>
38	2346	H	Cl	Cl	Cl	H	Cl	H	H	4.36	24.15	112.07	-2227.88	4.00	48.18	3.71	1.51	<b>-0.56</b>	<b>19.14</b>
39	2347	H	Cl	Cl	Cl	H	H	Cl	H	3.90	24.15	112.22	-2227.89	4.00	47.93	3.71	1.51	<b>-0.49</b>	<b>19.12</b>
40	2348	H	Cl	Cl	Cl	H	H	H	Cl	3.81	24.15	112.92	-2227.89	4.00	48.05	3.71	1.51	<b>-0.46</b>	<b>19.13</b>
41	2356	H	Cl	Cl	H	Cl	Cl	H	H	4.12	24.25	110.85	-2227.86	4.00	48.76	3.71	1.51	<b>-0.60</b>	<b>19.26</b>
42	2357	H	Cl	Cl	H	Cl	H	Cl	H	3.57	24.23	111.84	-2227.87	4.00	47.96	3.71	1.50	<b>-0.48</b>	<b>19.24</b>
43	2358	H	Cl	Cl	H	Cl	H	H	Cl	3.54	24.23	111.66	-2227.87	4.00	48.03	3.71	1.50	<b>-0.48</b>	<b>19.25</b>
44	2367	H	Cl	Cl	H	H	Cl	Cl	H	3.57	24.23	111.89	-2227.88	4.00	47.76	3.71	1.50	<b>-0.48</b>	<b>19.22</b>
45	2368	H	Cl	Cl	H	H	Cl	H	Cl	3.54	24.23	112.18	-2227.87	4.00	47.96	3.71	1.50	<b>-0.47</b>	<b>19.24</b>
46	2378	H	Cl	Cl	H	H	H	Cl	Cl	3.44	24.30	111.54	-2227.88	4.00	47.61	3.71	1.50	<b>-0.49</b>	<b>19.27</b>
47	2456	H	Cl	H	Cl	Cl	Cl	H	H	4.16	24.25	110.32	-2227.85	4.00	48.68	3.71	1.51	<b>-0.62</b>	<b>19.25</b>
48	2457	H	Cl	H	Cl	Cl	H	Cl	H	3.61	24.23	111.04	-2227.87	4.00	47.78	3.71	1.50	<b>-0.51</b>	<b>19.23</b>
49	2458	H	Cl	H	Cl	Cl	H	H	Cl	3.62	24.23	111.24	-2227.87	4.00	47.95	3.71	1.50	<b>-0.51</b>	<b>19.24</b>
50	2467	H	Cl	H	Cl	H	Cl	Cl	H	3.61	24.23	111.46	-2227.87	4.00	47.68	3.71	1.50	<b>-0.50</b>	<b>19.22</b>
51	2468	H	Cl	H	Cl	H	Cl	H	Cl	3.62	24.23	111.68	-2227.87	4.00	47.86	3.71	1.50	<b>-0.49</b>	<b>24.03</b>
52	2478	H	Cl	H	Cl	H	H	Cl	Cl	3.52	24.23	111.22	-2227.87	4.00	47.56	3.71	1.50	<b>-0.49</b>	<b>19.21</b>
53	2567	H	Cl	H	H	Cl	Cl	Cl	H	3.48	24.33	109.87	-2227.86	4.00	48.49	3.71	1.50	<b>-0.56</b>	<b>19.36</b>
54	2568	H	Cl	H	H	Cl	Cl	H	Cl	3.56	24.33	110.17	-2227.86	4.00	48.66	3.71	1.50	<b>-0.56</b>	<b>19.37</b>
55	2578	H	Cl	H	H	Cl	H	Cl	Cl	3.37	24.31	110.85	-2227.89	4.00	48.27	3.71	1.50	<b>-0.51</b>	<b>19.33</b>
56	2678	H	Cl	H	H	H	Cl	Cl	Cl	3.37	24.31	110.65	-2227.87	4.00	47.63	3.71	1.50	<b>-0.51</b>	<b>19.28</b>
57	3456	H	H	Cl	Cl	Cl	Cl	H	H	4.11	24.15	111.55	-2227.86	4.00	48.11	3.71	1.51	<b>-0.54</b>	<b>19.13</b>
58	3457	H	H	Cl	Cl	Cl	H	Cl	H	3.78	24.13	112.27	-2227.87	4.00	47.24	3.71	1.50	<b>-0.47</b>	<b>19.11</b>
59	3458	H	H	Cl	Cl	Cl	H	H	Cl	3.94	24.13	112.75	-2227.87	4.00	47.48	3.71	1.50	<b>-0.48</b>	<b>19.12</b>
60	3467	H	H	Cl	Cl	H	Cl	Cl	H	3.78	24.13	112.87	-2227.88	4.00	47.18	3.71	1.50	<b>-0.45</b>	<b>19.10</b>
61	3468	H	H	Cl	Cl	H	Cl	H	Cl	3.94	24.13	113.48	-2227.89	4.00	47.69	3.71	1.50	<b>-0.45</b>	<b>19.14</b>
62	3478	H	H	Cl	Cl	H	H	Cl	Cl	4.05	24.13	112.37	-2227.87	4.00	46.99	3.71	1.50	<b>-0.50</b>	<b>19.09</b>
63	3567	H	H	Cl	H	Cl	Cl	Cl	H	3.26	24.23	110.81	-2227.86	4.00	47.97	3.71	1.50	<b>-0.47</b>	<b>19.24</b>
64	3568	H	H	Cl	H	Cl	Cl	H	Cl	3.48	24.23	106.84	-2227.84	4.00	45.39	3.71	1.50	<b>-0.63</b>	<b>19.05</b>
65	3578	H	H	Cl	H	Cl	H	Cl	Cl	3.51	24.21	111.24	-2227.87	4.00	47.25	3.71	1.50	<b>-0.49</b>	<b>19.17</b>
66	3678	H	H	Cl	H	H	Cl	Cl	Cl	3.51	24.21	111.97	-2227.87	4.00	47.19	3.71	1.50	<b>-0.46</b>	<b>19.17</b>
67	4567	H	H	H	Cl	Cl	Cl	Cl	H	3.26	24.23	110.82	-2227.86	4.00	47.97	3.71	1.50	<b>-0.47</b>	<b>19.24</b>
68	4568	H	H	H	Cl	Cl	Cl	H	Cl	3.26	24.23	111.27	-2227.86	4.00	48.20	3.71	1.50	<b>-0.45</b>	<b>19.26</b>
69	4578	H	H	H	Cl	Cl	H	Cl	Cl	3.55	24.21	111.38	-2227.87	4.00	47.28	3.71	1.50	<b>-0.49</b>	<b>19.17</b>
70	4678	H	H	H	Cl	H	Cl	Cl	Cl	3.55	24.21	111.89	-2227.87	4.00	47.18	3.71	1.50	<b>-0.47</b>	<b>19.17</b>
71	5678	H	H	H	H	Cl	Cl	Cl	Cl	3.20	24.31	109.79	-2227.86	4.00	47.95	3.71	1.50	<b>-0.52</b>	<b>19.30</b>

Table 1:-Predicted values of Log(LC<sub>50</sub>)and BCF of 70 molecules obtained from chlordane.



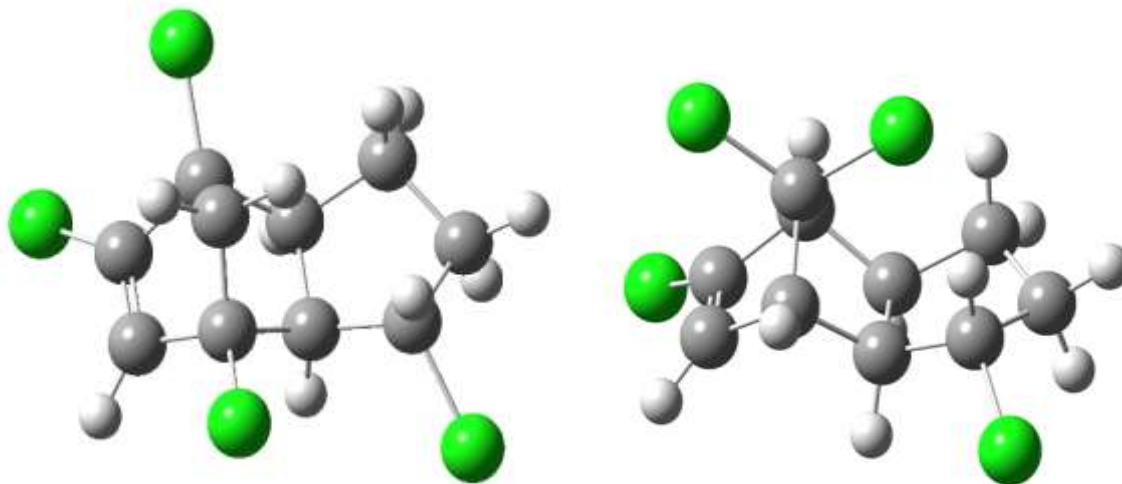
**Figure 2:-** Structure of chlordane with the position of each chloride atoms highlighted.

After an analysis of Table 1, we notice that the molecules with index 1238 and 3568 have the better characteristics than the remaining molecules. These molecules are displayed in Table 2.

**Table 2:-** Molecules proposed displaying the best values of  $\log LC_{50}$  and BCF.

N°	Index	Nature of atoms as a function of positions								$\log LC_{50}$	BCF
		1	2	3	4	5	6	7	8		
1	1238	Cl	Cl	Cl	H	H	H	H	Cl	-0.41	19.25
2	3568	H	H	Cl	H	Cl	Cl	H	Cl	-0.63	19.05

It shows that the first molecule ("1238") has the largest value of toxicity ( $\log LC_{50} = -0.41$ ). The second molecule ("3568") presents the the smallest values of bioconcentration factor and toxicity ( $BCF = 19.05$ ;  $\log LC_{50} = -0.63$ ). The first molecule is therefore the least active (the least toxic) and the second is the most active (the most toxic) but the least bioaccumulative. The structures of both molecules are shown in Figure 3.



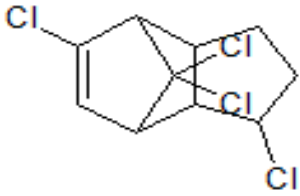
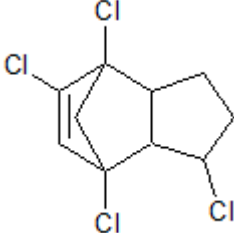
**Figure 3:-** Structures of "3568" (on the left) and "1238"(on the right).

#### Theoretical characterization of "3568" and "1238"

Table 3 provides some parameters of the proposed molecules. The characterization of these molecules was carried out with Gaussian 03 [26] and ChemSketch [27] programs.

**Table 3:-** Values of some parameters of molecules "3568" and "1238".

Parameters	Values	
Code	3568	1238

Structure		
Name of molecule (proposed by ChemSketch)	(1S,2S,3R,6R,7R)-3,8,10,10-tetrachlorotricyclo[5.2.1.0 <sup>2,6</sup> ]dec-8-ene	1R,2R,3R,6R,7S)-3,8,7,8-tetrachlorotricyclo[5.2.1.0 <sup>2,6</sup> ]dec-8-ene
Molecular formula	C <sub>10</sub> H <sub>10</sub> Cl <sub>4</sub>	C <sub>10</sub> H <sub>10</sub> Cl <sub>4</sub>
Composition	C(44.16%) H(3.71%) Cl(52.14%)	C(44.16%) H(3.71%) Cl(52.14%)
Formula weight	272g/mol	272g/mol
	3.48 ± 0.37	3.13 ± 0.38
Molecular refractivity	61.13 ± 0.4 cm <sup>3</sup>	61.18 ± 0.4 cm <sup>3</sup>
Molecular volume	180.5 ± 5.0 cm <sup>3</sup>	179.7 ± 5.0 cm <sup>3</sup>
Index of refraction	1.59 ± 0.03	1.60 ± 0.03
Surface tension	45.0 ± 5.0 dyne/cm	46.0 ± 5.0 dyne/cm
Density	1.50 ± 0.1 g/cm <sup>3</sup>	1.51 ± 0.1 g/cm <sup>3</sup>
Polarisability	24.23 ± 0.5 10 <sup>-24</sup> cm <sup>3</sup>	24.25 ± 0.5 10 <sup>-24</sup> cm <sup>3</sup>
	0.26(Cal/Mol)	0.26(Cal/Mol)
	0.03(Cal/Mol)	0.03(Cal/Mol)
	45.39 Cal/Mol-Kelvin	48.63 Cal/Mol-Kelvin
Entropy (S)		112.176(Cal/Mol – Kelvin)
Dipole moment	1.48 Debye	2.12 Debye

We can see that both molecules are isomers of configuration. Therefore, they seem different by their dipole moment.

### Substitution effect of four atoms of chlorine by atoms of fluorine on the chlordane molecule

#### Analysis of the results

To check the effect of the halogens on the chlordane, we have used the molecules "3568" and "1238" on which we substituted four atoms of hydrogen by four atoms of fluorine. The new molecules obtained are named respectively "tetrafluorochlordane 1" and tetrafluorochlordane 2" and proposed in Figure 4. These molecules were optimized at the B3LYP/6-31++g(d,p) level using the Gaussian 03 software [26]. The QSAR and QSPR models proposed respectively by equations (1) and (2) are used to determine the values of  $\log LC50$  and  $BCF$ .

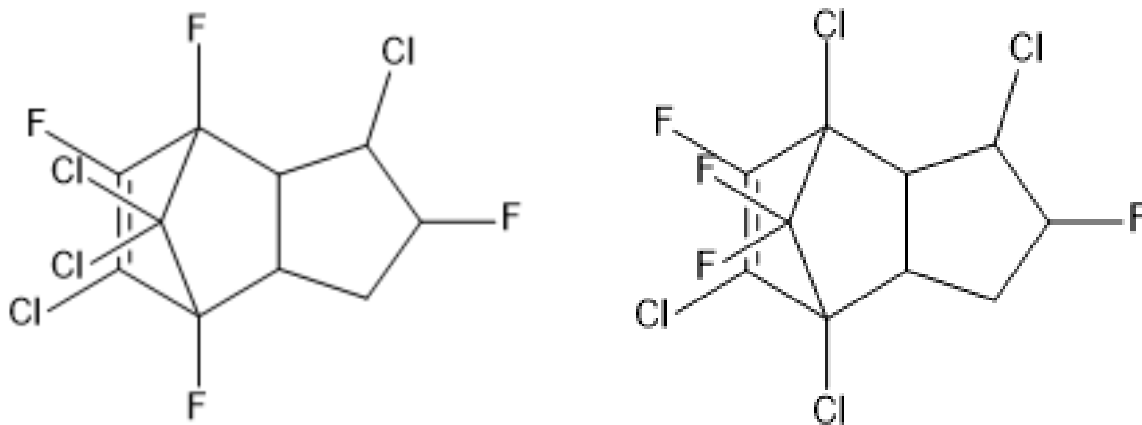


Figure 4:- Structures of tetrafluorochlordane 1 (a) and tetrafluorochlordane 2(b).

The comparison on one hand between the value of  $\log LC_{50}$  and on other hand between the value of BCF shows that the four new molecules ("1238", "3568", tétrafluorochlordane 1 and tétrafluorochlordane 2) are biologically active. Because the determined values of  $\log LC_{50}$  for these four molecules belong the interval set by the values recorded with the chlordane and the fluordane which are assumed to be also biologically active (see table 4). The molecule "3568" is the most active of the four molecules proposed and the molecule "tétrafluorochlordane 2" is the least active. However, the molecule more accumulable is "tétrafluorochlordane 1" and "3568" is less accumulable.

**Tableau 4:-** Values of descriptors,  $\log LC_{50}$  and BCF of chlordane, "3568", "1238", "tétrafluorochlordane 1", "tétrafluorochlordane 2" and Fluordane.

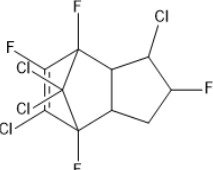
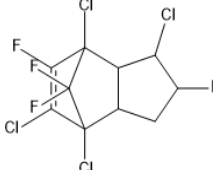
Molécule	$\log P$	$\alpha$	$S$	$ZPE$	$N_{Cl}$	$C_V$	%H	$d$	$\log LC_{50}$	BCF
Chlordane	5.57	31.82	136.53	-4066.37	8.00	63.32	1.48	1.80	-2.59	26.32
"3568"	3.48	24.23	106.84	-2227.83	4.00	45.39	3.71	1.50	-0.63	19.05
"1238"	3.13	24.25	112.18	-2227.89	4.00	48.63	3.71	1.51	-0.41	19.25
"tétrafluorochlordane 1"	3.98	24.34	127.84	-2624.94	4.00	59.63	1.76	1.71	0.16	20.38
"tétrafluorochlordane 2"	3.60	24.34	127.30	-2624.97	4.00	59.16	1.76	1.71	0.20	20.34
Fluordane					0				0.8 <sup>a</sup>	

From Table 4 it can be understood that fluorine reduces the toxicity of organochlorine compounds but increases their bioaccumulation factor. Which confirms the statement of Murphy's team [28]. Indeed, these researchers reported that organofluorine compounds can persist in the environment. However, these compounds are generally inert compounds that are more polar (less hydrophobic) than organochlorines, thus suggesting less toxicity [19]. In consequence, they are assumed to display more asset that justifies their great use as pesticides (herbicides, fungicides and insecticides) [22].

#### Theoretical characterization of "tetrafluorochlordane 1" and "tetrafluorochlordane 2"

Table 5 provides some parameters of the proposed molecules obtained with gaussian 03 [26] and ChemSketch [27] software.

**Tableau 5:-** Values of some parameters of "tetrafluorochlordane 1" and "tetrafluorochlordane 2".

Paramètre	Valeur	
	tétrafluorochlordane 1	tétrafluorochlordane 2
Code		
Structure		
Name of molecule (proposed by ChemSketch)	(1R,2S,3S,4R,6R,7S)-3,8,10,10-tétrachloro-1,4,7,9-tétrafluorotricyclo[5,2,1,0 <sup>2,6</sup> ]dec-8-ene	(1S,2S,3R,4S,6S,7S)-1,3,7,8-tétrachloro-4,9,10,10-tétrafluorotricyclo[5,2,1,0 <sup>2,6</sup> ]dec-8-ene
Molecular formula	C <sub>10</sub> H <sub>6</sub> Cl <sub>4</sub> F <sub>4</sub>	C <sub>10</sub> H <sub>6</sub> Cl <sub>4</sub> F <sub>4</sub>
Composition	C(34,92%) H(1,76%) Cl(41,23%) F(22,09%)	C(34,92%) H(1,76%) Cl(41,23%) F(22,09%)
Formula weight	343,9g/mol	343,9g/mol
	3,98 ± 0,68	3,60 ± 0,65
Molecular refractivity	61,41 ± 0,4 cm <sup>3</sup>	61,41 ± 0,4 cm <sup>3</sup>
Molecular volume	201,0 ± 5,0 cm <sup>3</sup>	201,0 ± 5,0 cm <sup>3</sup>
Index of refraction	1,522 ± 0,03	1,522 ± 0,03
Surface tension	36,7 ± 5,0 dyne/cm	36,7 ± 5,0 dyne/cm
Density	1,71 ± 0,1 g/cm <sup>3</sup>	1,71 ± 0,1 g/cm <sup>3</sup>
Polarisability	24,34 ± 0,5 10 <sup>-24</sup> cm <sup>3</sup>	24,34 ± 0,5 10 <sup>-24</sup> cm <sup>3</sup>
	0,28 Cal/Mol	-0,28 Cal/Mol
	0,06 Cal/Mol	-0,05 Cal/Mol

	45,39Cal/Mol-Kelvin	59,16 Cal/Mol-Kelvin
Entropy (S)		127,30( $\frac{Cal}{Mol - Kelvin}$ )
Dipole moment	2,31 Debye	2,11Debye

### Conclusion:-

In this study, we have used QSAR and QSPR models and based on the fact that the compounds which have more than four chlorine atoms are persistent to propose new molecules to replace the chlordane. This study allowed to propose four molecules which are: (1S,2S,3R,6R,7R)-3,8,10,10-tétrachlorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene known by "3568", (1R,2R,3R,6R,7S)-3,8,7,8-tétrachloro-tricyclo[5.2.1.0<sup>2,6</sup>]dec-8-ene) which index is "1238", (1R,2S,3S,4R,6R,7S)-3,8,10,10-tétrachloro-1,4,7,9-tetrafluorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene) called tetrafluorochlordane 1 and (1S,2S,3R,4S,6S,7S)-1,3,7,8-tétrachloro-4,9,10,10- tétrafluorotricyclo[5,2,1,0<sup>2,6</sup>]dec-8-ene) that state for tétrafluorochlordane 2. The first two are those which present the best values of  $\log(LC50)$  and  $BCF$  among the seventy molecules that we have proposed. The other two are those which were obtained from the first two but by substituting hydrogen atoms by fluorine atoms. This showed the effect of fluorine on chlordane. Considering the values of calculated properties, we can say that these different molecules are biologically active. But organofluorine compounds would be the most suitable as to replace the organochlorine compounds. These molecules have been characterized theoretically using ChemSketch and Gaussian 03. This characterization can be used for the synthesis of this molecule in order to verify its insecticide, herbicide, fungicide or other activities.

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