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Methyltetraprole (MTP) is a new mitotoxic agent aiming at blocking complex III of the mitochondrial respiratory chain. It is proposed as a substitute for strobilurins which also act at the QoI (Quinone outside inhibitor) site of complex III. Indeed, the extensive use of strobilurins has led to the rapid appearance of resistance which now makes their use ineffective in a large part of Europe.

From a strictly scientific point of view, it appears that:

1) Like most mitotoxic agents targeting the respiratory chain, a pathway extremely conserved during evolution for these essential elements including complex III, it is perfectly clear that the action of this type of substance cannot have any selectivity for a given species simply because of the identity of the mode of action. At best, we will observe, for the few species used for the tests, a sometimes lower sensitivity. This sensitivity will vary greatly depending on media (air, land, water, etc.), routes of exposure, timing of developmental exposures (for humans, infants, elderly, etc.), durations and finally, the frequency of exposure according to the state of health of the organisms exposed, including humans. It should be noted that in the case of MTP, these crucial factors, taken in isolation but even more so in groups, have not been studied.

2) As demonstrated for strobilurins, or other mitotoxic agents such as SDHIs, due to the resistance appearing in the targeted microorganisms, the use of such substances is bound to fail for farmers within a few years. The failure of this use has proven to be concomitant with now well-recognized ecological consequences affecting firstly the microflora and microfauna of the soil, then the multiple associated trophic chains, including humans. The appearance of multi-drug resistant microorganisms can also represent an uncontrollable danger for the entire biosphere.

3) As the SDHI studies (SDHI are mitotoxics acting on complex II of the mitochondrial respiratory chain) have shown, tests carried out on human cells in culture (the only ones carried out on human material) will be completely defective in detecting the mitotoxicity of a substance such as MTP. This inadequacy is now recognized in France by ANSES. Added to this defective nature of the cellular tests is the serious incompleteness of the genotoxicity tests. Indeed, on the one hand, dealing with the nuclear genes, only major rearrangements are considered, whereas the mitotoxic agents affecting the respiratory chain are known to be able just as much to cause occasional oxidative modifications of DNA without necessarily going as far as to major overhauls. On the other hand, the genes carried by the DNA present in the mitochondria are not even studied. These genes are however the first concerned by the oxidative stress caused by mitotoxic agents such as MTP. It should be noted that, in a cell, these genes, never studied, represent, due to the number of mitochondria in a cell and their repetition in each mitochondrion, as many if not more genes, than those carried by the nuclear DNA.

4) The toxicity of MTP, like that of all pesticides, should now imperatively be tested under realistic conditions, i.e. in the context of the well-known cocktail effect which can only increase with the steady introduction of new pesticides. Incidentally, this omnipresence of many pesticides now makes scientifically serious epidemiological studies extremely difficult, if not impossible, except for very specific cases.

In conclusion, introducing a new substance like MTP into the environment appears irresponsible in view of current scientific knowledge and of the limits when it comes to the guarantees that we scientists are able to provide. For information, ANSES has been informed of this opinion, which is shared by many colleagues, but did not oppose any scientific argument to justify the introduction of the MTP.

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