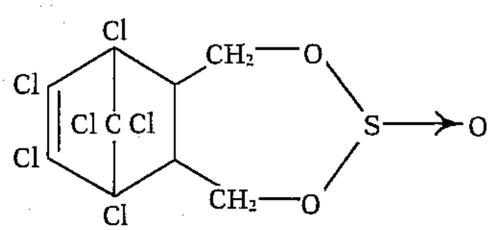
Dr. OESER
Farbwerke Hoechst AG - Analystisches Laboratorium - Frankfurt (Main)

THE RESIDUE BEHAVIOUR OF ENDOSULFAN AND ITS DECOMPOSITION IN WARM-BLOODED ANIMALS

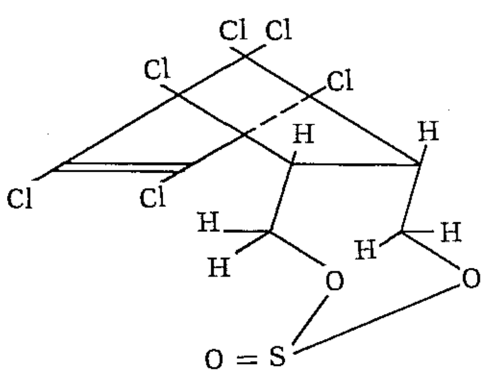
The insecticide endosulfan serves for the control of bitting and sucking insects on fruits and plants in agriculture and forestry. It has a great advantage over many other insecticides in that it is non-toxic to bees; it is therefore used above all in orchards and in the seed growing of cabbage, clover and lucerne, etc.

Technical endosulfan is a mixture of two stereoisomers of hexachloro-bicycloheptene-bis-(methylene)-sulphite which are designated α- and β-endosulfan (fig. 1). The isomers can be determined by the position of the SO-bands in the infra-red spectrum (α-endosulfan 1192 cm^{-1}, β-endosulfan 1180 cm^{-1}) [3, 4], and also by gas chromatography.

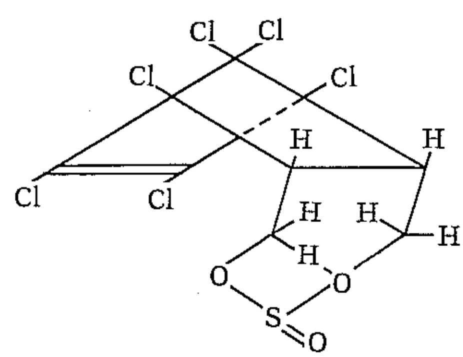
Fig. 1 - *Endosulfan (Thiodan ®).*



Endosulfan (Thiodan ®)



α - Endosulfan



β - Endosulfan

The ratio of isomers in the technical product is roughly 70% α- to 30% β-endosulfan. The acute oral LD_{50} for rats for α-endosulfan is 76, in the case of β-endosulfan it is 240 and for the technical active ingredient it is about 100 mg/kg body weight [2]. The acute dermal LD_{50} for rats is 680, for rabbits 147 and for guinea-pigs more than 1000 mg/kg [6].

As regards the persistence of endosulfan isomers on the plant, it was found that the α-isomer disappears faster than the β-isomer. An example for this is the testing of endosulfan residues which were formed on the grass of meadows as a result of drift during the control of chockchafers by spraying neighbouring deciduous forests from helicopters [7].

TABLE 1 - Decomposition of α- and β-endosulfan on the grass of meadows

Days after application	Contents of the grass (ppm)		
	α	β	α+β
0	1.3	0.5	1.8
7	0.15	0.12	0.3
14	0.04	0.07	0.1

In the endosulfan residue the ratio of α- to β-endosulfan shifts in the course of 14 days from 70:30 to 35:65. We made this observation on various plants and fruits, e. g. maize, apples, pears; it is attributable to the considerably higher vapour pressure of α-endosulfan.

To be able to compare as independently as possible from the plant growth, the decomposition rate of endosulfan on live plants with that of certain insecticides from the series of «chlorinated hydrocarbons», pastures whose growth was complete were sprayed with comparable concentrations of other active ingredient formulations [8]. Fig. 2 shows the results. Of Toxaphen® and DDT®, less than 70% were degraded and 84% of the Aldrin, whereas 92 and 94% respectively of endosulfan and lindane were degraded.

The endosulfan residues were thus found to be less persistent than the insecticides Toxapen, DDT and Aldrin and were approximately equal in persistence to the residues of lindane.

In the residue analysis by gas chromatography of endosulfan, besides the aforementioned peaks of α- and β-endosulfan, a third peak of unknown origin was found [7]. It was conspicuous that this peak was not detectable in the chromatograms which were obtained from extracts immediately following the endosulfan application, whereas it temporarily occurred in higher amounts in samples taken subsequently. It was found that this was a transformation product formed on the surface of the leaves, i. e. endosulfan sulphate (we use the not quite correct term «endosulfan sulphate» for the oxidation product formed according to >S=O

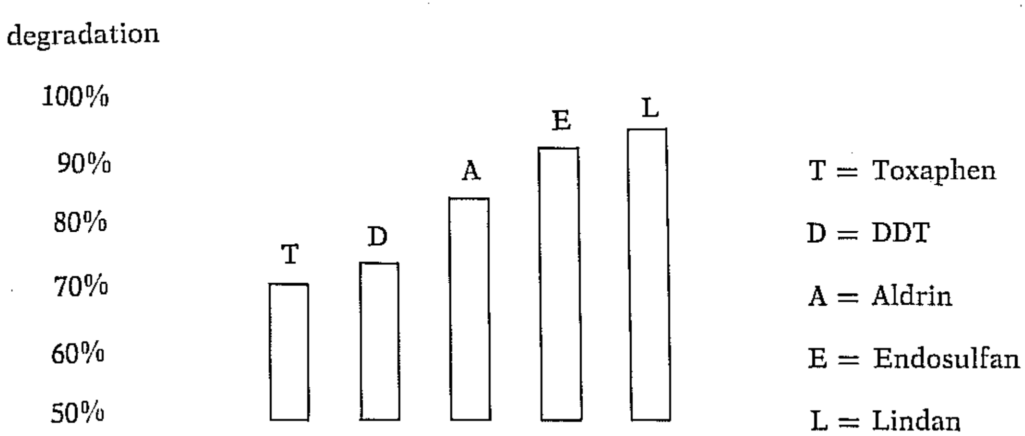


Fig. 2 - *The decomposition of various insecticides 14 days after spraying.*

TABLE 2 - The decomposition of endosulfan on cotton leaves

	Trial No.	Residues in ug/cm² of learf surface Days after application		
		0	3	5
Ethiopia	1	2.21		0.09
	2	1.96		0.08
	3	2.42		0.15
	4	1.51		0.09
	5	1.08		0.06
Brazil	1	3.11	0.04	0.24
	2	2.93	0,30	0.26
	3	4.13		0.06
	4	3.36		0.15

$\rightarrow >SO_2$). It is the sulphuric acid ester of the sulphurous acid ester endosulfan, i. e. its oxidation product [1].

In recent years, we carried out trials for combating insects, especially butterfly larvae and eggs on cotton plants in Brazil and Ethiopia. The data in table 2 show a similarly rapid active ingredient decrease, as we have already shown by means of the preceding table. The active ingredient content fell within 5 days of treatment from 1.86 and 3.38 to 0.04 and 0.18 ug/cm² of leaf surface respectively (average values).

When we had observed the reduction of endosulfan on plants by way of measuring the residues, the question arose as to the persistence of the active ingredient in the soil. We had to clarify whether endosulfan accumulates in the soil or whether it gets into the water table with the rain.

In the first test series this question of accumulation was examined in field trials. For this purpose 600 litres/hectare of a 0.4% endosulfan emulsion were applied and the active ingredient content of the soil tested after 0, 2, 5, 13, 22, and 50 weeks.

TABLE 3 - The decomposition of endosulfan in the soil

	Residues in ppm Weeks after application					
	0	2	5	13	22	50
α-endosulfan	0.5	0.2	0.1	0.04	0.03	0.02
β-endosulfan	0.4	0.3	0.1	0.03	0.03	0.01
endosulfan sulphate	0.2	0.1	0.07	—	0.04	0.08
Σ endosulfan	1.1	0.6	0.3	0.27	0.10	0.11

Table 3 shows only a small part of our test results; a loamy, sandy soil was concerned; we obtained virtually the same results on loam.

To make sure that the active ingredient had not migrated into lower strata of the soil, the samples used for the 50-week values were taken from various soil depths (table 4).

It has been conclusively proved by these tests that no accumulation of endosulfan takes place in the soil and that there is no migration into deeper soil layers.

The question still to be clarified was whether endosulfan can be washed into the water table by rain, thereby possibly contributing towards contamination of the drinking water with crop protection chemicals. For this purpose the rain-water was

TABLE 4 - Endosulfan residues subdivided into different soil depths

	Residues (ppm) in different soil depths (cm)		
	0-5	5-15	15-75
α-endosulfan	0.02	0.03	0.02
β-endosulfan	0.002	0.006	n.d.
endosulfan sulphate	0.004	n.d.	n.d.
Σ endosulfan	0.026	0.036	0.02

analysed in several lysimeter tests after passing through 1 m^3 of soil. The active ingredient had been applied to the soil in two different concentrations (1.2 and 2.4 kg/hectare). During the course of a whole year no endosulfan was detectable in the water, the limit of detection of α-, β-endosulfan and endosulfan sulphate being 0.002 ppm.

To determine whether endosulfan is stored in the organism of warmblooded animals or whether it is excreted unchanged or is metabolized, we conducted experiments on milk sheep who were given 15 mg of endosulfan per day (equivalent to 2 ppm in the feed) over a period of 26 days [5]. Dieldrin served as the comparison preparation which was administered in the same concentration and for the same period of time.

After six days already, the milk exhibited 3 ppm of dieldrin whilst during the entire 26-day period no α- or β-endosulfan was detectable in the milk. Only small amounts (0.1 ppm) of a decomposition product were detected which were found to be endosulfan sulphate.

About 20% of the ingested active ingredient was excreted unchanged in the faeces.

No endosulfan was detectable in the urine, whereas several metabolites were found to be present, one of which was identified as endosulfan alcohol (1 ppm) (see fig. 3).

After completion of the experiments we examined the following organs and tissue samples: liver, kidney, brain tissue, muscle fibre, intestinal fat and renal fat. No endosulfan was detectable in any of the samples. Small amounts of endosulfan sulphate were detected in the fatty tissue. The situation was different in the animals which had been given dieldrin. As shown in fig. 4, up to 20 ppm of dieldrin were detected, and the organs also exhibited notable amounts of dieldrin.

Investigations of Maier-Bode with sows confirm our trials. Feed with a 2 ppm active ingredient content (this corresponds to the US tolerance) was given for 27, 54 and 81 days. DDT served as the comparison preparation (7 ppm corresponds to the US tolerance).

These experiments confirm that endosulfan in contrast to the other insecticides is not stored in the organism of warm-blooded animals. Although endosulfan sulphate was present in small amounts as a residue, its toxicological appraisal corresponds to that of endosulfan. Under normal conditions of feeding, no amounts objectionable from a toxicological aspect are to be expected in the milk of animals (<0.1 ppm).

I should like to refer briefly to the toxicology of endosulfan. Ten years ago already,

Fig. 3.

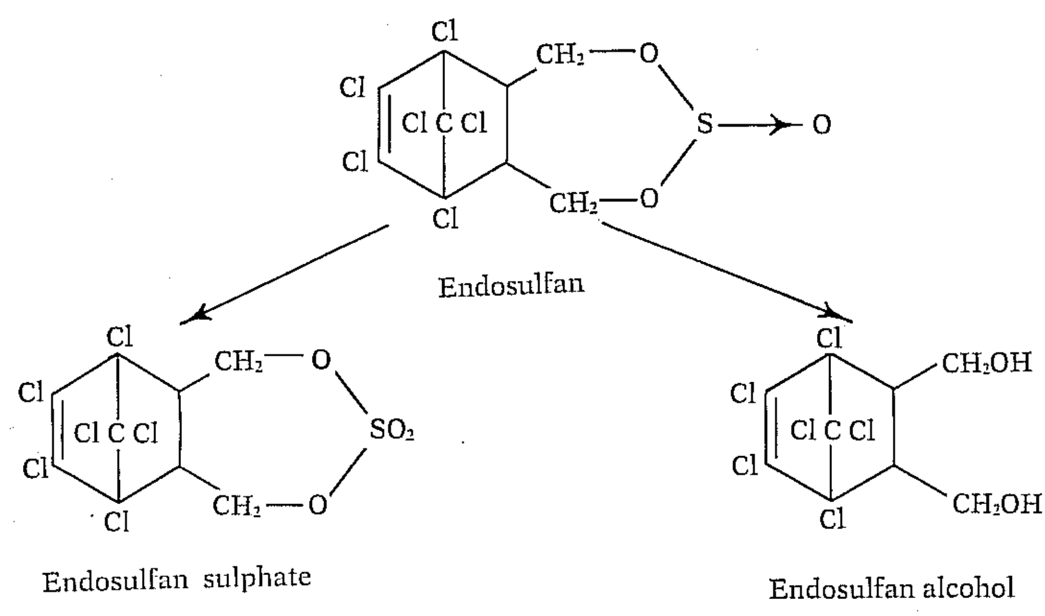
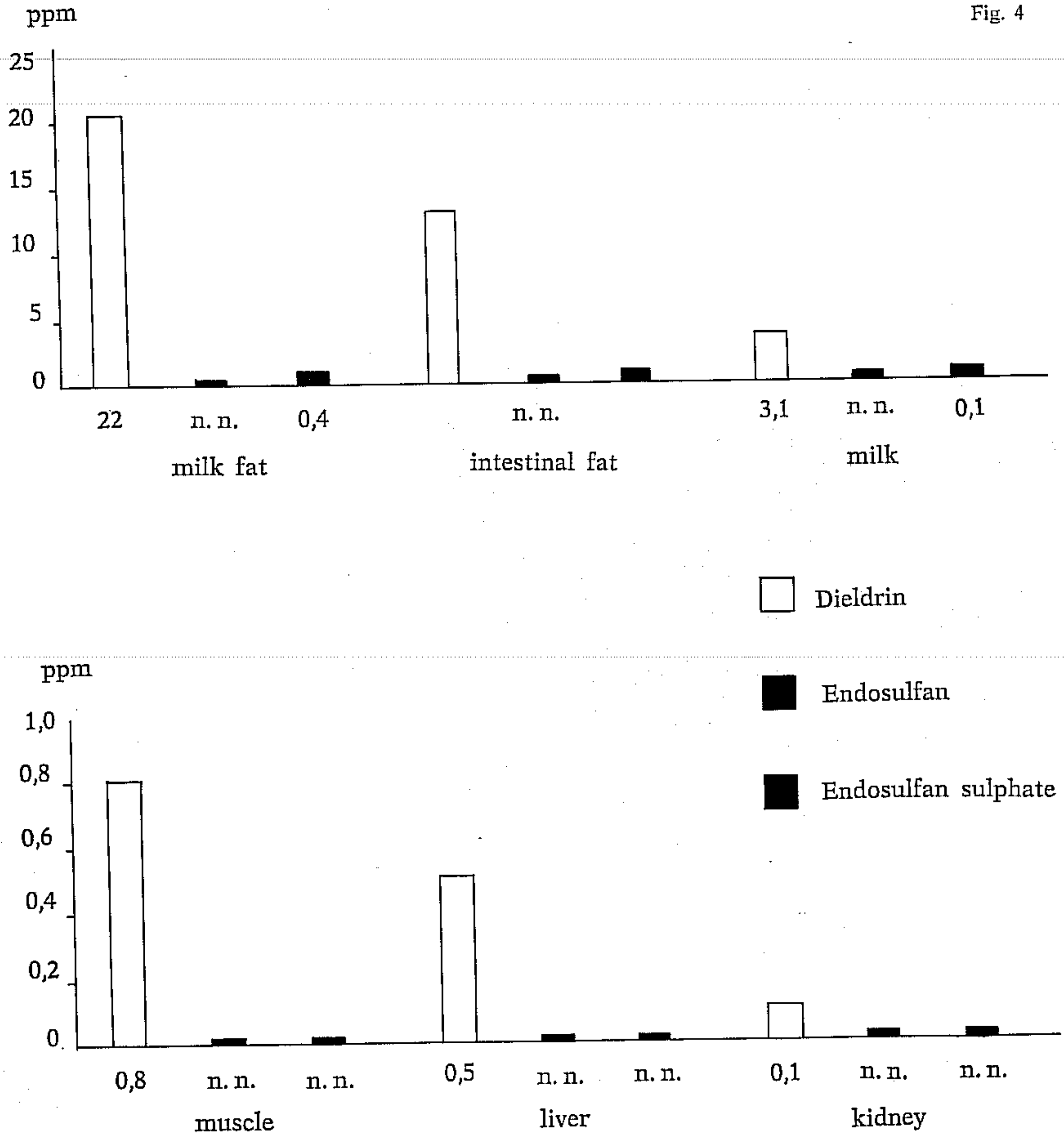


Fig. 4



Hazleton Laboratories Incorporated, Falls Church, Virginia, made available to us the study on the 2-year feeding test (= long-term toxicity test) with technical endosulfan in the rat. It was found that the highest dose added to the daily ration of the animals which did not show any signs of toxicity or pharmacological effect in the rats, was 30 ppm. 1 ppm of an active ingredient in the feed of the rat is equivalent to 0.05 mg/kg rat/day. Since the rat tolerates the daily endosulfan dose of 30 ppm administered with its feed, without sustaining any deleterious effects on its organism, a «no effect level» of this preparation for the rat is found to be $0.05 \times 30 = 1.5$ mg/kg body weight. After taking into account a safety factor of 100, the tolerable dose for man in this case is 0.015 mg/kg body weight.

For conversion of these daily amounts in mg/kg body weight permissible for man, the international authorities premise that human beings ingest an average of about 0.4 kg of fresh fruit and fresh vegetables per day. At an average body weight of 60 kg, with a «no effect level» of endosulfan for man of 0.015 ppm, the resulting «maximum permissible residue amount» per day in man therefore is:

$$\frac{0.015 \text{ mg/kg} \times 60 \text{ kg}}{0.4 \text{ kg}} = 2.25 \text{ ppm.}$$

In 1965, Industrial Bio-Test Laboratories Inc., Northbrook, Illinois, also an internationally acknowledged body, furnished a report on the three-generation study they had conducted with endosulfan in rats. The following result was obtained:

In all rats of these three generations no deleterious effect was detectable which might be connected in any way with the oral administration of the preparation in amounts of 2 and 50 ppm respectively in the daily feed. From this it follows that the amount of endosulfan active ingredient administered with the feed that does not cause any signs of toxicity of pharmacological effect, is 50 ppm.

This value, like the afore-mentioned 2-year value of 30 ppm, was acknowledged for endosulfan by the Expert Committee of the World Health Organization (WHO) of the United Nations in 1968.

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RIASSUNTO

L'insetticida Endosulfan è una miscela di due isomeri, di cui quello con punto di fusione più basso è noto come α-Endosulfan e quello con punto di fusione più elevato come β-Endosulfan. Il rapporto degli isomeri nel prodotto tecnico è di circa 70% α-Endosulfan e 30% β-Endosulfan.

I residui di Endosulfan sulle superfici delle piante persistono meno che quelli del Toxaphen, del DDT e dell'Aldrin. L'α-Endosulfan scompare dalla superficie delle piante più rapidamente che β-Endosulfan. Come prodotto di trasformazione dell'Endosulfan su foglie e frutti è stato trovato il solfato di Endosulfan che tossicologicamente deve essere valutato come l'Endosulfan.

L'analisi dei residui dimostra che dopo 2-3 settimane vengono trovate meno di 0,5 ppm di residuo di Endosulfan (compreso il solfato di Endosulfan).

L'Endosulfan non si concentra nel terreno. Come dimostrano alcune prove eseguite su diversi tipi di terreno, dopo 50 settimane almeno il 90% era stato degradato. Le acque freatiche non vengono contaminate dall'Endosulfan. Si è analizzata per più di un anno l'acqua piovana, dopo aver passato 1 m³ di terreno su cui si era applicato da 1,2 a 2,4 kg di Endosulfan per ettaro. L'acqua non ha presentato tracce di Endosulfan.

Delle prove eseguite su animali a sangue caldo hanno dimostrato che una parte della sostanza attiva viene espulsa inalterata con le feci. Nell'urina sono stati reperiti dei metaboliti idrossolubili (solfato di Endosulfan e alcool di Endosulfan). Nel latte degli animali sono stati analizzati soltanto scarsi quantitativi di solfato di Endosulfan (0,1 ppm).

Contrariamente a quanto avviene con Dieldrin e DDT, l'Endosulfan non si accumula nel grasso degli animali a sangue caldo. Per 26 giorni consecutivi si è somministrato a delle pecore 15 mg di Endosulfan e rispettivamente di Dieldrin, per via orale. Trascorso il periodo di prova, nel grasso degli animali non era identificabile α- e β-Endosulfan e solo 0,1 ppm di solfato di Endosulfan, ma 13,7 ppm di Dieldrin.

Nella letteratura l'Endosulfan viene spesso in-

dicato nel gruppo degli «idrocarburi clorurati». Come è stato dimostrato da confronti con altre sostanze attive di questa classe, la differenza nella scarsa persistenza dell'Endosulfan sulla superficie di piante vive e la mancanza di accumulo nel grasso dell'organismo animale è così sostanziale che l'Endosulfan non può essere classificato in questo gruppo di sostanze attive.

SUMMARY

The insecticide endosulfan is a mixture of two isomers of which that with the lower melting point is called α-endosulfan and that with the higher melting point is called β-endosulfan. The ratio of the isomers in the technical product is about 70% α-and 30% β-endosulfan.

Residues of endosulfan are less persistent on plant surfaces than are residues of Toxaphen, DDT and Aldrin. α-Endosulfan disappears faster from plant surfaces than does β-endosulfan. Endosulfan sulphate was found as a transformation product of endosulfan on leaves and fruit. Toxicologically it has to be appraised like endosulfan.

The residue analysis shows that after 2 to 3 weeks less than 0.5 ppm of endosulfan residue (including endosulfan sulphate) is found.

Endosulfan does not accumulate in the soil. After 50 weeks, at least 90% had been decomposed, as was shown by tests conducted in various types of soil. The water table is not contaminated by endosulfan. For a period of more than a year the rain-water was analysed after passing through 1 m^3 of soil to which had been applied 1.2 and 2.4 kg respectively of endosulfan/hectare. No endosulfan was detectable in the water.

Tests in warm-blooded animals showed that part of the active ingredient is excreted in the faeces. Water-soluble metabolites (endosulfan sulphate and endosulfan alcohol) were detected in the urine. Only small amounts of endosulfan sulphate (0.1 ppm) were analysed in the milk.

In contrast to dieldrin and DDT, endosulfan is not stored in the fat of warm-blooded animals. On 26 consecutive days sheep were given 15 mg of endosulfan and dieldrin respectively by mouth. At the end of the trial period, no α- or β-endosulfan and only 0.1 ppm of endosulfan sulphate was detected in the fat of the animals, whereas 13.7 ppm of dieldrin were found.

In the literature, endosulfan is often classed among the group of «chlorinated hydrocarbons».

As shown by comparisons with other active ingredients of this series, the difference between the low persistence of endosulfan on the surface of live plants and the absence of storage in the fat of the animal organism is so considerable that endosulfan cannot be classed with this group of active ingredients.