

# Chemical, Toxicological, and Biological Properties of Endothall

OBREN KECKEMET

*Pennwalt Corporation  
Tacoma, Washington*

Endothall was first discovered as having herbicidal properties by Tischler, *et al* (8) in 1950 when the defoliant and desiccant properties were described for terrestrial plants. The aquatic herbicidal properties were discovered in 1953 (5) and it was first registered for this use in 1960.

## CHEMISTRY

Endothall\* has commonly been called 3,6-endoxohexahydrophthalic acid but the proper nomenclature is 7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid. It is related to cantharidic acid, a chemical found in nature, and unlike almost all other pesticide chemicals it contains only carbon, hydrogen, and oxygen (Figure 1).



Figure 1. Chemical structure of endothall (left) and cantharidic acid (right).

Endothall is not applied as the free acid but is converted to its inorganic or amine salts. The most active salts are: 1. Disodium endothall; 2. Dipotassium endothall; 3. Mono- and di-(N,N-dimethylalkylamine) endothall; 4. Mono- and di-(N,N-dimethyltridecyclamine) endothall.

Highest herbicidal activity occurs in the amine salts having 12 to 16 carbons. (5). Short chain amine salts are less active. It was established early in the development of endothall that defoliant activity on terrestrial plant foliage was accelerated by the addition of ammonium sulfate, but this is not true for soil or aquatic applications (5).

The endothall salts are supplied as water concentrates for aquatic use. It is not necessary to use organic solvents or emulsifiers. The tradename for the sodium and potassium salts is AQUATHOL® and for the fatty amine salts HYDROTHOL®. Both control a variety of aquatic weeds. HYDROTHOL, in addition, controls several types of algae. The average recommended use rate for AQUATHOL is 2 to 3 ppmw for large or total area treatment with a maximum of 5 ppmw for marginal or spot treatment. Recommended use of HYDROTHOL covers a range of 0.05 to 4 ppmw.

Hundreds of endothall derivatives have been synthesized, but to date none have been found significantly more active than the original structure (5). Many salts and esters were prepared and a few are superior with regard to the spectrum of susceptible weeds and degree of activity. Many

\*Name approved by the American Standards Association.

were also found to be more toxic to fish, but some encouraging leads are now being followed.

## ANIMAL TOXICITY

The study of the toxicity of disodium endothall and related salts began in 1951 and still continues.

The oral LD<sub>50</sub> rates for disodium endothall formulation (AQUATHOL) (15.5% endothall) is 198 mg/kg and for technical endothall is 51 mg/kg. The oral LD<sub>50</sub> of di-(N,N-dimethylalkylamine) salt of endothall (HYDROTHOL 47) (containing 28% endothall) is 206 mg/kg for rats. Subacute toxicity studies with sodium endothall for four months in the diet of dogs revealed no harmful effect at 1,000 ppm (6). HYDROTHOL 47 was not harmful at 108 ppm, the highest concentration tested (6).

Radioactive endothall administered orally to rats at 50 ppm in the feed was eliminated completely from all tissues and organs within 72 hours. Endothall was not found in milk nor fat, nor was it transferred through the milk pathway to the feeding pups. (6).

It has been demonstrated in the long term (chronic) feeding studies in rats and dogs and three generation studies in rats that the apparent "no harmful effect" dosage level for disodium endothall in the most sensitive animal tested (the rat) is in excess of 300 ppm in the diet (6). This dosage level would be equivalent to a total daily intake of 750 mg per day for a 50 kg human. Based on a one kilogram per day diet, this represents the equivalent to eating one-half of the daily food intake having a residue of 1,500 parts per million of disodium endothall.

This level after being extrapolated to residues in water where a person consumes 2 kg of water on day of application, all of which contains endothall residues, would mean that 3.75 ppm would not constitute a hazard when normally acceptable safety factor of 100 to 1 is used. An additional important safety factor is that endothall residues in water have rapid biological breakdown with smaller amounts being consumed each day for only a few days per year. This is in contrast to products with long residual life which would be consumed over a long period of time.

## TOXICITY TO FISH AND WATER ORGANISMS

The inorganic salts (sodium and potassium) of endothall are safe to fish in concentrations of 100 to 800 ppm. To quote one of our leading fish biologists: "Endothall, because of its low toxicity to fish, low toxicity to the eggs or fry, and the rates of aquatic use, appears to be one of the safest herbicides to use during spawning season. In addition, the toxicity of endothall in water is of relatively short duration." (3).

On the other hand, long chain amine salts are toxic to fish under laboratory conditions at concentrations of 0.5 to

3 ppmw (10). It is interesting that these amine salts are two to three times more active on aquatic weeds than inorganic salts and 200 to 400 times more toxic to fish. However, these amine salts have been employed in practice with little, if any, fish kill because: 1. A portion of the chemical is quickly adsorbed and decomposed by plants and soil; 2. For control of algae rates below those toxic to fish are employed; 3. Label recommendations are to treat lakes or ponds in sections at a time rather than overall bodies of water. 4. Fish detect presence of these amine salts and move from treated areas; 5. In irrigation canals concentrations decrease rapidly due to movement of water.

On oysters and clams the inorganic salts (the only ones tested) are safe at 5 to 10 ppm. Endothall is the safest aquatic herbicide on *Daphnia*, besides 2,4-D and potassium salt of silvex. Other fish food organisms are not affected at all by normal rates of either type of endothall salt formulation.

### MECHANISM OF ACTION

It has been established that in terrestrial plants, endothall is not translocated. It is a typical contact type, membrane active, compound. Endothall induces callose formations in parenchyma, epidermal, and mesophyll cells. This results in abnormal permeability with breakdown of the osmotic system, rapid loss of water, wilting, and rapid desiccation of tissues (4).

Behavior of endothall is not exactly the same in aquatic plants due to difference in function of various plant organs and environment. When  $^{14}\text{C}$  endothall is applied to winter buds of *Potamogeton nodosus*  $^{14}\text{C}$  can be observed in apical leaves, buds and roots of secondary plants. Movement was not observed when applied to the *Potamogeton nodosus* roots. Translocation in *Elodea canadensis* is apparently limited. Endothall greatly accelerates protoplasmic rotation in *Elodea canadensis* leaf cells. The exact reasons for this are not known, though some hypotheses have been formed. Chloroplasts become smaller and yellowish. A disintegration of the lipoprotein complex of the membrane system is indicated. An interesting finding is that *Elodea canadensis* metabolizes endothall considerably more rapidly than *Potamogeton nodosus*. This may explain relative resistance of one species and relative susceptibility of another. (4, 7, 9)

### PERSISTENCE

It was clearly demonstrated in vitro that many species of bacteria and fungi normally inhabiting all soils and waters break the endothall molecule and utilize its fragments as a source of carbon. This was reconfirmed in field practice. Beets, spinach, aquatic plants, and those species of fish, studied break down endothall rapidly and completely. The biodegradation process is influenced by temperature, soil moisture, etc. Endothall, as such, disappears completely from the soil one to three weeks after application and from water one to ten days after application. Accordingly, endothall can be considered a highly biodegradable compound. (5).

Studies by Freed *et al* (2) concluded that "plants, fish, and soil microorganisms are capable of completely metabolizing endothall." It is assumed that the endoxo bridge is the first point of attack. It appears that breakdown fractions of endothall are utilized by the biochemical system of organisms and finally released in the form of carbon

dioxide. Metabolic products of endothall do not appear to accumulate, but further work is underway (2).

### RESIDUE ANALYTICAL PROCEDURES

Under present pesticide laws it is mandatory that chemical residues in any agricultural commodity be known and be within set tolerances. It is known from radioactive studies and bioassays that endothall residues on crops or in water are zero a relatively short time after application.

The establishment of a tolerance for endothall required submission of a sensitive chemical analytical method. The development of such a method has been hampered by the unique structure of endothall. The only elements present are carbon, H, and O which are in a structural form difficult to isolate in minute quantities from living matter. Most pesticide chemicals contain at least another element such as halogens, phosphorus, sulfur, or nitrogen to assist in detection. In addition, certain breakdown products appear to be carboxylic acids commonly found in biological organisms, particularly in plant tissues.

Efforts are being intensified to increase the sensitivity of a chemical analytical procedure and it is certain that this can now be achieved with the new instrumentation available. A gas chromatographic method is available where few interfering substances are present. This method is accurate to 0.005 ppm and is useful for analyzing water samples and technical material.

### SUMMARY

Endothall has unique aquatic herbicidal properties which can be summarized as follows:

1. It is effective on many submersed aquatic weeds.
2. It is highly biodegradable, since no persistent residues of endothall or metabolites accumulate.
3. The inorganic salts have a minimum 20 to 1 safety factor between weed and fish kill.
4. The amine salts when used as directed cause little, if any, fish kill.
5. Endothall is not harmful to beneficial organisms in the aquatic environment.
6. Extensive animal studies indicate that 3.75 ppm in water is not harmful in the diet when the 100 to 1 safety factor is used.

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