

A screening-level environmental assessment of macrocyclic fragrance materials

D. T. Salvito¹; B. Parkhurst³; C. L. McIntosh²; C. Sachse-Vasquez¹

¹RIFM, Woodcliff Lake, NJ, USA. ²Firmenich, Inc., Princeton, NJ, USA. ³HAF, Inc., Laramie, WY, USA.

A screening-level aquatic ecological risk assessment for macrocyclic fragrance materials using a group approach is presented. In the group approach, conservative environmental fate and effects values for compounds within the structure-activity group are used to estimate the potential for aquatic ecological risks for the group as a whole. The results of the screening-level aquatic ecological risk assessment indicate that at their current volume of use in Europe and North America, macrocyclic fragrance materials pose a negligible risk to aquatic biota. This negligible risk is primarily a function of two factors: (1) macrocyclic fragrance materials are readily biodegradable and are efficiently removed in wastewater treatment plants, and (2) their aquatic toxicity is low.

Introduction

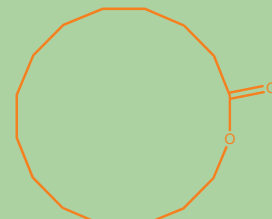
The RIFM Environmental Framework was developed as a screening tool by the Research Institute for Fragrance Materials (RIFM) to screen through a large database of organic compounds used as fragrance ingredients to assess their potential environmental risk and set priorities for further risk assessment, as necessary. RIFM has historically used structure activity groups for the assessment of human health safety. Presented here is the first application of a group approach for the aquatic risk assessment of a structurally related group of fragrance ingredients. This group analysis of the macrocyclic fragrance ingredients described below is appropriate because the data available for the group as a whole and individually support the concept that these materials are not only structurally related but behave similarly in the aquatic environment. In the group approach, conservative environmental fate and effects values for individual compounds within the group are used to estimate the potential for aquatic ecological risks for the group as a whole.

Chemical Structures

Ketone



Lactone



- ▶ 10 materials – 6 with unsaturation on ring
- ▶ 3 with methyl side chain
- ▶ Ring ranges from 14 to 17 carbons
- ▶ Log Kow range: 4.98 to 6.31 (est.)

- ▶ 11 materials – 4 with unsaturation on ring
- ▶ No side chains
- ▶ Ring ranges from 14 to 16 carbons
- ▶ Log Kow range: 4.22 to 6.7(est.)

Environmental Effects and Risks

- ◆ Available measured endpoints:
 - ▶ Biodegradation studies for materials in both groups
 - ▶ Ecotox data:
 - Ketones: 3-Methylcyclopentadecanone
 - Lactones/Lactides:
 - ◆ Ethylene brassylate
 - ◆ Ethylene dodecanedioate
 - ◆ Oxacyclohexadecen-2-one
- ◆ PEC/PNEC estimation by group

Biodegradation Summary: Ketones

- ◆ 12 studies on 4 materials
 - ▶ 3-Methylcyclopentadecanone - 7 studies
 - ▶ Z-4-Cyclopentadecen-1-one - 2 studies
 - ▶ 5-Cyclohexadecen-1-one - 2 studies
 - ▶ Cyclopentadecanone - 1 study
- ◆ Minimally 28 day tests
- ◆ Conclusion: Macrocyclic ketones exhibit a high rate of removal in wastewater treatment and are readily biodegradable

Lactone/Lactide Biodegradation Summary

Material	Method	Result
Ethylene brassylate	301F	89%
Ethylene brassylate	301F	77%
Ethylene brassylate	301F	73%
Ethylene brassylate	"Closed Bottle"	40%*
Ethylene brassylate	301B	>100%
Ethylene brassylate	301F	89%
Ethylene brassylate	301C	85% (BOD) 100% (GC)
ω-Pentadecalactone	301B	93%
Ethylene dodecanedioate	301B	114%
Ethylene dodecanedioate	301C	73% (BOD) 100% (GC)
Ethylene dodecanedioate	301B	80% & 78%
Oxacyclohexadecen-2-one	SCAS	99.3% removal
Oxacyclohexadecen-2-one	301C	92% (BOD) 100% (GC)
Oxacyclohexadecen-2-one	301B	86.1% & 87.1%
Oxacyclohexadecen-2-one	301F	95%
Oxacycloheptadec-10-ene-2-one	301F	84%

- ◆ The results indicate that these chemicals are readily biodegradable and therefore are not expected to persist in the environment.

Ketone Biodegradation Summary

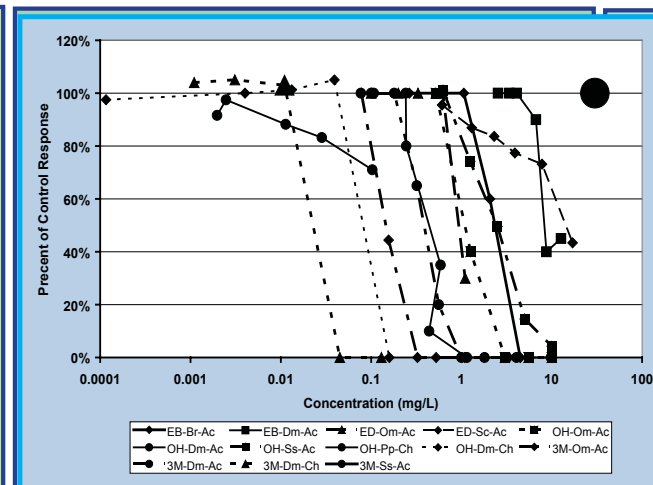
MATERIAL	METHOD	RESULT
3-Methylcyclopentadecanone	SCAS	99.9% removal
3-Methylcyclopentadecanone	301F	61%
3-Methylcyclopentadecanone	301D	43%*
3-Methylcyclopentadecanone	301B	78.8%
3-Methylcyclopentadecanone	302A	96.1% removal
3-Methylcyclopentadecanone	302C	85% (BOD) 100% (GC)
3-Methylcyclopentadecanone	301B	93.4% & 96.4%
Z-4-Cyclopentadecen-1-one	302A	99.8% removal
Z-4-Cyclopentadecen-1-one	301B	83.9%
5-Cyclohexadecen-1-one	302C	60%
5-Cyclohexadecen-1-one	301C	52%, 60%, & 68%
Cyclopentadecanone	302A	66.7%

Biodegradation Summary: Lactones/Lactides

- ◆ 16 studies on 5 materials
 - ▶ Ethylene dodecanedioate - 3 studies
 - ▶ Ethylene brassylate - 7 studies
 - ▶ Oxacyclohexadecen-2-one - 4 studies
 - ▶ ω-Pentadecalactone - 1 study
 - ▶ Oxacycloheptadec-10-ene-2-one - 1 study
- ◆ Minimally 28 day tests
- ◆ Conclusion: Macrocyclic lactones and lactides exhibit a high rate of removal in wastewater treatment and are readily biodegradable

Ecotoxicological Data Summary

- ◆ Ketones - 7 studies on 1 material
 - ▶ 3-methylcyclopentadecanone
 - Aquatic(4)/Terrestrial(3)
- ◆ Lactones/Lactides - 14 studies on 3 materials
 - ▶ Ethylene dodecanedioate-3 studies
 - All aquatic
 - ▶ Ethylene brassylate-3 studies
 - Aquatic(2)/Sludge(1)
 - ▶ Oxacyclohexadecen-2-one-8 studies
 - Aquatic(5)/Terrestrial(2)/Sediment(1)



Acute and chronic toxicity data for macrocyclic fragrance materials. The figure legend is as follows: EB-Br-Ac = ethylene brassylate, *Brachydanio rerio*, acute test; EB-Dm-Ac = ethylene brassylate, *Daphnia magna*, acute test; ED-Om-Ac = ethylene dodecanoate, *Onchorhynchus mykiss*, acute test; ED-Sc-Ac = ethylene dodecanoate, *Selenastrum capricornutum*, acute test; OH-Om-Ac = oxacyclohexadecen-2-one, *Onchorhynchus mykiss*, acute test; OH-Dm-Ac = oxacyclohexadecen-2-one, *Daphnia magna*, acute test; OH-Ss-Ac = oxacyclohexadecen-2-one, *Scenedesmus subspicatus*, acute test; OH-Pp-Ch = oxacyclohexadecen-2-one, *Pimephales promelas*, chronic test; OH-Dm-Ch = oxacyclohexadecen-2-one, *Daphnia magna*, chronic test; 3M-Om-Ac = 3-methylcyclopentadecanone, *Onchorhynchus mykiss*, acute test; 3M-Dm-Ac = 3-methylcyclopentadecanone, *Daphnia magna*, chronic test; 3M-Dm-Ch = 3-methylcyclopentadecanone, *Daphnia magna*, chronic test; 3M-Ss-Ac = 3-methylcyclopentadecanone, *Scenedesmus subspicatus*, acute test. The minimum NOEC is indicated with a large solid triangle, while the maximum NOEC is indicated with a large solid circle.

Summary of acute and chronic toxicity data for macrocyclic fragrance materials

OECD Test Method [3]	Chemical	Species	Exposure Method	Most Sensitive Endpoint	Exposure Duration (days)	LC50/EC50, Measured Concentration (mg/L)	NOEC, Measured Concentration (mg/L)
201	3-Methylcyclopentadecanone	<i>Scenedesmus subspicatus</i>	Static	Growth	3	>30	30
202	Ethylene Dodecanoate	<i>Daphnia magna</i>	Static	Mobilization	2	>14	14
202	Ethylene Brassylate	<i>Daphnia magna</i>	Static	Mobilization	2	Not determined	4.09
203	Ethylene Brassylate	<i>Brachydanio rerio</i>	Static	Survival	4	Not determined	1.0625
201	Oxacyclohexadecen-2-one	<i>Scenedesmus subspicatus</i>	Static	Growth	3	2.4	0.625
203	Ethylene Dodecanoate	<i>Onchorhynchus mykiss</i>	Flow-Through	Survival	4	0.88	0.62
201	Ethylene Dodecanoate	<i>Selenastrum capricornutum</i>	Static	Growth	3	1.7	0.61
203	Oxacyclohexadecen-2-one	<i>Onchorhynchus mykiss</i>	Flow-Through	Behavior	4	2	0.52
202	Oxacyclohexadecen-2-one	<i>Daphnia magna</i>	Static	Mobilization	2	0.48	0.242
202	3-Methylcyclopentadecanone	<i>Daphnia magna</i>	Static	Mobilization	2	0.39	0.18
203	3-Methylcyclopentadecanone	<i>Onchorhynchus mykiss</i>	Static-Renewal	Behavior	4	0.22	0.078
211	Oxacyclohexadecen-2-one	<i>Daphnia magna</i>	Static-Renewal	Reproduction	21	Not determined	0.0392
210	Oxacyclohexadecen-2-one	<i>Pimephales promelas</i>	Flow-Through	Weight	33	Not determined	0.0285
211	3-Methylcyclopentadecanone	<i>Daphnia magna</i>	Static-Renewal	Reproduction	21	Not determined	0.011

PEC/PNEC Estimation

- ◆ Basis: RIFM Framework- European scenario
- ◆ RQ estimated on a group basis
 - ▶ Separate RQs estimated for ketones and lactones/lactides
- ◆ Group exposure estimate:
 - ▶ Highest volume (Europe)
 - ▶ Readily biodegradable
 - ▶ Highest log K_{ow}
- ◆ Lowest aquatic endpoint for group
- ◆ Assessment factor applied:
 - ▶ Ketones (3 acutes/2 chronics): 50
 - ▶ Lactones/Lactides (3 acutes/3 chronics): 10

Group	Ketones	Lactones/Lactides
Volume (EU)	<10 tonnes	>100 tonnes
Log K _{ow}	6.3	6.7
Biodegradability Rate	3/hr	3/hr
MW used	250.43	256.39
NOEC	0.011 mg/L (<i>D. magna</i>)	0.027 mg/L (<i>P. promelas</i>)
AF	50	10
PNEC	0.22 ug/L	2.7 ug/L
RQ	<0.1	<0.1

- ◆ The screening level risk quotient for the aquatic compartment was well below 0.1, indicating that the macrocyclic fragrance ingredients do not present an environmental risk at their current use levels.

Summary

- ◆ Macrocyclic fragrance ingredients are readily biodegradable and well removed from wastewater treatment plants
- ◆ A screening level risk assessment indicates that macrocyclic fragrance ingredients do not pose an environmental risk to the aquatic compartment
- ◆ Sediment and terrestrial toxicity studies to date show that these materials are not highly toxic in these compartments
- ◆ Peer-reviewed publication is in preparation summarizing these data

References

Salvito, DT, Senna, RJ, Federle, TW. 2002. A framework for prioritizing fragrance materials for aquatic risk assessment. *Environ Toxicol Chem*: 21: 301-1308.

Bickers, DR, Calow, P, Greim, HA, Hanifin, JM, Rogers, AE, Saurat, J-H, Sipes, IG, Smith, RL and Tagami, H. The safety assessment of fragrance materials. *Regulatory Toxicology and Pharmacology*, 37(2), 218-273.