

AOP: 175 - Thyroperoxidase inhibition leading to altered amphibian metamorphosis
Dose-response and temporal concordance evaluation table
Values indicate lowest observed effect level

Time point (d)	Reference	Chemical Initiator	In vivo concentrations tested	MIE	KE1				KE2	KE3	KE4	AO	Compensatory responses					
				TPO inhibition (IC50)	Thyocytes: Synthesis decreased		T4 in serum,		Tissue T4,	Tissue T3,	Metamorphosis,	Thyroid gland	Serum TSH,	NIS	Thyroid follicular cell	Thyroidal iodide,		
				AUR	GU	MIT	DTT	T3	T4	decreased	decreased	decreased	altered	histopathology	increased	upregulation	number increased	increased
in vitro	Paul et al. 2014	Methimazole	-	0.025 uM (2.85 µg/l)	2.2 uM (251 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-
in vitro	Paul Friedman et al. 2016	Methimazole	-	0.06 uM (6.84 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
in vitro	Tietze et al. 2013	Methimazole	-	-	0.67 uM (76 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-
in vitro	Hornung et al. 2015	Methimazole	-	-	1 uM (114 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-
NF51 + 8d	Degitz et al. 2005	Methimazole	6.25, 12.5, 25, 50, 100 mg/l	-	-	-	-	-	-	-	-	-	-	12.5 mg/l	-	-	-	-
NF54 + 1d	Tietze et al. 2010	Methimazole	100 mg/l	-	n/s	n/s	-	n/s	n/s	-	-	-	n/s	-	-	n/s	-	-
NF54 + 2d	Tietze et al. 2010	Methimazole	100 mg/l	-	100 mg/l	100 mg/l	100 mg/l	100 mg/l	n/s	-	-	-	n/s	100 mg/l	-	n/s	n/s	-
NF54 + 2d	Haselman et al. 2020	Methimazole	6.25, 12.5, 25 mg/l	-	12.5 mg/l	12.5 mg/l	12.5 mg/l	12.5 mg/l	n/s	-	-	-	-	-	n/s	n/s	-	-
NF54 + 4d	Tietze et al. 2010	Methimazole	100 mg/l	-	100 mg/l	100 mg/l	100 mg/l	100 mg/l	n/s	-	-	-	n/s	100 mg/l	-	n/s	n/s	-
NF54 + 4d	Haselman et al. 2020	Methimazole	6.25, 12.5, 25 mg/l	-	12.5 mg/l	6.25 mg/l	6.25 mg/l	6.25 mg/l	n/s	-	-	-	-	-	12.5 mg/l	n/s	-	-
NF54 + 6d	Tietze et al. 2010	Methimazole	100 mg/l	-	100 mg/l	100 mg/l	100 mg/l	100 mg/l	100 mg/l	-	-	-	n/s	100 mg/l	-	n/s	-	-
NF54 + 7d	Haselman et al. 2020	Methimazole	6.25, 12.5, 25 mg/l	-	6.25 mg/l	12.5 mg/l	12.5 mg/l	6.25 mg/l	12.5 mg/l	-	-	-	-	-	12.5 mg/l	n/s	-	-
NF54 + 8d	Tietze et al. 2010	Methimazole	100 mg/l	-	-	-	-	-	-	-	-	-	-	100 mg/l	-	100 mg/l	-	-
NF54 + 8d	Degitz et al. 2005	Methimazole	6.25, 12.5, 25, 50, 100 mg/l	-	-	-	-	-	-	-	-	-	-	6.25 mg/l	-	-	-	-
NF54 + 10d	Haselman et al. 2020	Methimazole	6.25, 12.5, 25 mg/l	-	12.5 mg/l	12.5 mg/l	12.5 mg/l	6.25 mg/l	6.25 mg/l	-	-	-	-	-	6.25 mg/l	6.25 mg/l	6.25 mg/l	-
NF51 + 14d	Degitz et al. 2005	Methimazole	6.25, 12.5, 25, 50, 100 mg/l	-	-	-	-	-	-	-	-	-	25 mg/l	-	-	-	-	-
NF54 + 14d	Degitz et al. 2005	Methimazole	6.25, 12.5, 25, 50, 100 mg/l	-	-	-	-	-	-	-	-	-	25 mg/l	-	-	-	-	-
NF51 + 21d	Coady et al. 2010	Methimazole	4, 16.5, 50 mg/l	-	-	-	-	-	-	-	-	-	4 mg/l	-	-	-	-	-
NF54 → NF62	Haselman et al. 2020	Methimazole	6.25, 12.5, 25 mg/l	-	-	-	-	-	-	-	-	-	6.25 mg/l	-	-	-	-	-
in vitro	Paul et al. 2014	6-propylthiouracil	-	0.12 uM (20 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
NF51 + 8d	Degitz et al. 2005	6-propylthiouracil	1.25, 2.5, 5, 10, 20 mg/l	-	-	-	-	-	-	-	-	-	-	5 mg/l	-	-	-	-
NF54 + 1d	Tietze et al. 2010	6-propylthiouracil	20 mg/l	-	n/s	n/s	-	n/s	n/s	-	-	-	n/s	-	-	n/s	-	-
NF54 + 2d	Tietze et al. 2010	6-propylthiouracil	20 mg/l	-	20 mg/l	20 mg/l	-	20 mg/l	20 mg/l	-	-	-	n/s	20 mg/l	-	n/s	n/s	-
NF54 + 2d	Haselman et al. 2020	6-propylthiouracil	2.22, 6.67, 20 mg/l	-	n/s	20 mg/l	n/s	n/s	n/s	-	-	-	-	-	n/s	n/s	-	-
NF54 + 4d	Tietze et al. 2010	6-propylthiouracil	20 mg/l	-	n/s	20 mg/l	-	20 mg/l	n/s	-	-	-	n/s	20 mg/l	-	n/s	n/s	-
NF54 + 4d	Haselman et al. 2020	6-propylthiouracil	2.22, 6.67, 20 mg/l	-	n/s	6.67 mg/l	2.22 mg/l	6.67 mg/l	n/s	-	-	-	-	-	20 mg/l	n/s	n/s	-
NF54 + 6d	Tietze et al. 2010	6-propylthiouracil	20 mg/l	-	n/s	20 mg/l	-	20 mg/l	20 mg/l	-	-	-	n/s	20 mg/l	-	n/s	n/s	-
NF54 + 7d	Haselman et al. 2020	6-propylthiouracil	2.22, 6.67, 20 mg/l	-	n/s	n/s	n/s	20 mg/l	n/s	-	-	-	-	-	20 mg/l	20 mg/l	20 mg/l	-
NF54 + 8d	Tietze et al. 2010	6-propylthiouracil	20 mg/l	-	-	-	-	-	-	-	-	-	-	20 mg/l	-	20 mg/l	20 mg/l	-
NF54 + 8d	Degitz et al. 2005	6-propylthiouracil	1.25, 2.5, 5, 10, 20 mg/l	-	-	-	-	-	-	-	-	-	-	5 mg/l	-	-	-	-
NF54 + 10d	Haselman et al. 2020	6-propylthiouracil	2.22, 6.67, 20 mg/l	-	6.67 mg/l	n/s	6.67 mg/l	n/s	n/s	-	-	-	-	-	20 mg/l	20 mg/l	20 mg/l	-
NF51 + 14d	Degitz et al. 2005	6-propylthiouracil	1.25, 2.5, 5, 10, 20 mg/l	-	-	-	-	-	-	-	-	-	10 mg/l	-	-	-	-	-
NF54 + 14d	Degitz et al. 2005	6-propylthiouracil	1.25, 2.5, 5, 10, 20 mg/l	-	-	-	-	-	-	-	-	-	20 mg/l	-	-	-	-	-
NF54 + 14d	Degitz et al. 2005	6-propylthiouracil	1.25, 2.5, 5, 10, 20 mg/l	-	-	-	-	-	-	-	-	-	10 mg/l	-	-	-	-	-
NF51 + 21d	Degitz et al. 2005	6-propylthiouracil	1.25, 2.5, 5, 10, 20 mg/l	-	-	-	-	-	-	-	-	-	20 mg/l	-	-	-	-	-
NF54 → NF62	Haselman et al. 2020	6-propylthiouracil	2.22, 6.67, 20 mg/l	-	-	-	-	-	-	-	-	-	20 mg/l	-	-	-	-	-
in vitro	Paul et al. 2014	2-Mercaptobenzothiazole	-	0.45 uM (75 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
in vitro	Tietze et al. 2013	2-Mercaptobenzothiazole	-	-	16.8 uM (2810 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-
in vitro	Hornung et al. 2015	2-Mercaptobenzothiazole	-	-	12 uM (2097 µg/l)	-	-	-	-	-	-	-	-	-	-	-	-	-
NF54 + 2d	Haselman et al. 2020	2-Mercaptobenzothiazole	30, 90, 270 µg/l	-	-	n/s	n/s	n/s	n/s	n/s	-	-	-	-	n/s	n/s	-	82 µg/l
NF54 + 4d	Haselman et al. 2020	2-Mercaptobenzothiazole	30, 90, 270 µg/l	-	-	n/s	270 µg/l	n/s	30 µg/l	n/s	-	-	-	-	90 µg/l	n/s	-	-
NF54 + 7d	Tietze et al. 2013	2-Mercaptobenzothiazole	18, 37, 82, 174, 357 µg/l	-	174 µg/l	82 µg/l	18 µg/l	18 µg/l	174 µg/l	-	-	-	n/s	18 µg/l	82 µg/l	37 µg/l	-	82 µg/l
NF54 + 7d	Hornung et al. 2015	2-Mercaptobenzothiazole	335 µg/l	-	335 µg/l	335 µg/l	335 µg/l	335 µg/l	335 µg/l	-	-	-	-	-	335 µg/l	-	-	-
NF54 + 7d	Haselman et al. 2020	2-Mercaptobenzothiazole	30, 90, 270 µg/l	-	n/s	270 µg/l	n/s	30 µg/l	n/s	-	-	-	-	-	30 µg/l	90 µg/l	-	-
NF54 + 10d	Haselman et al. 2020	2-Mercaptobenzothiazole	30, 90, 270 µg/l	-	n/s	270 µg/l	n/s	90 µg/l	270 µg/l	-	-	-	-	-	270 µg/l	90 µg/l	-	-
NF51 + 21d	Tietze et al. 2013	2-Mercaptobenzothiazole	23, 47, 109, 214, 435 µg/l	-	-	-	-	-	-	-	-	-	109 µg/l	23 µg/l	-	-	-	-
NF54 → NF62	Haselman et al. 2020	2-Mercaptobenzothiazole	30, 90, 270 µg/l	-	-	-	-	-	-	-	-	-	270 µg/l	-	-	-	-	-

Yellow highlight indicates earliest time point at which the effect was observed for each chemical initiator

Dashes - not applicable

n/s - not significant

NF - Nieuwekoop and Faber developmental stage

AUR - Amplex UltraRed

GU - Guaiacol

MIT - Monodiodotyrosine

DTT - Dithiodityrosine

T3 - Triiodothyronine

T4 - Thyroxine

TSH - Thyroid stimulating hormone

NIS - Sodium iodide symporter

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