

Introduction and Aims

- Citalopram, Fluoxetine, Sertraline - selective serotonin reuptake inhibitors (SSRIs),
- Duloxetine - serotonin and noradrenaline reuptake inhibitor (SNRI),
- Dosulepin - tricyclic antidepressant (TCA),

Widely prescribed and frequently detected in surface waters.

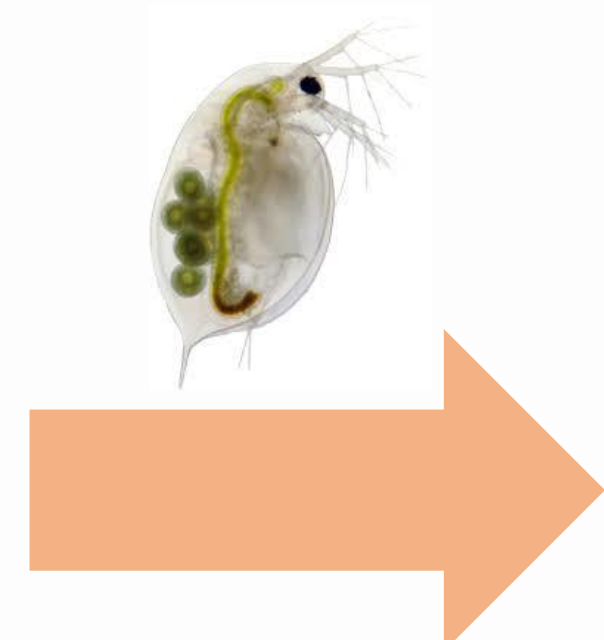
However, only limited information is available on its *in vivo* toxicity, particularly in invertebrates, under changing water pH.

- The overall aim of this study was therefore to establish the effects of pH on the acute and chronic toxicity of commonly used antidepressants to *Daphnia magna*
- The underlying hypotheses was that, given their pKa values, the toxicity of each antidepressants would increase with increasing pH value

Materials & Methods

pH 5.5, 6.0, 7.0, 7.5, 8.0 and 9.0

Citalopram - pKa = 9.78
Fluoxetine - pKa = 9.80
Sertraline - pKa = 9.56
Duloxetine - pKa = 9.70
Dosulepin - pKa = 9.76



48h Acute test (OECD TG 202)

21d Chronic test (OECD TG 211)

Results

- Mortality (48h)
- Reproduction (21d)
- Growth (21d)
- Toxicity prediction model

Fraction of ionization (Henderson-Hasselbalch equation)

Figure 1. Experimental design for the antidepressant toxicity test with *Daphnia magna*

Results

1. Fraction of ionic species (Henderson-Hasselbalch equation)

Table 1. Fraction of ionic species of the antidepressants at test pH values

pH	Uncharged ion distribution (%)				
	SSRIs (pKa)		SNRI (pKa)	TCA (pKa)	
	Citalopram (9.78)	Fluoxetine (9.80)	Duloxetine (9.70)	Sertraline (9.56)	Dosulepin (9.76)
5.5	0.00	0.00	0.01	0.01	0.01
6.0	0.02	0.02	0.03	0.02	0.02
7.0	0.16	0.16	0.27	0.2	0.17
7.5	0.52	0.50	0.86	0.62	0.55
8.0	1.61	1.55	2.66	1.94	1.71
9.0	14.1	13.6	21.5	16.6	14.8

2. 48h *D. magna* immobilisation tests

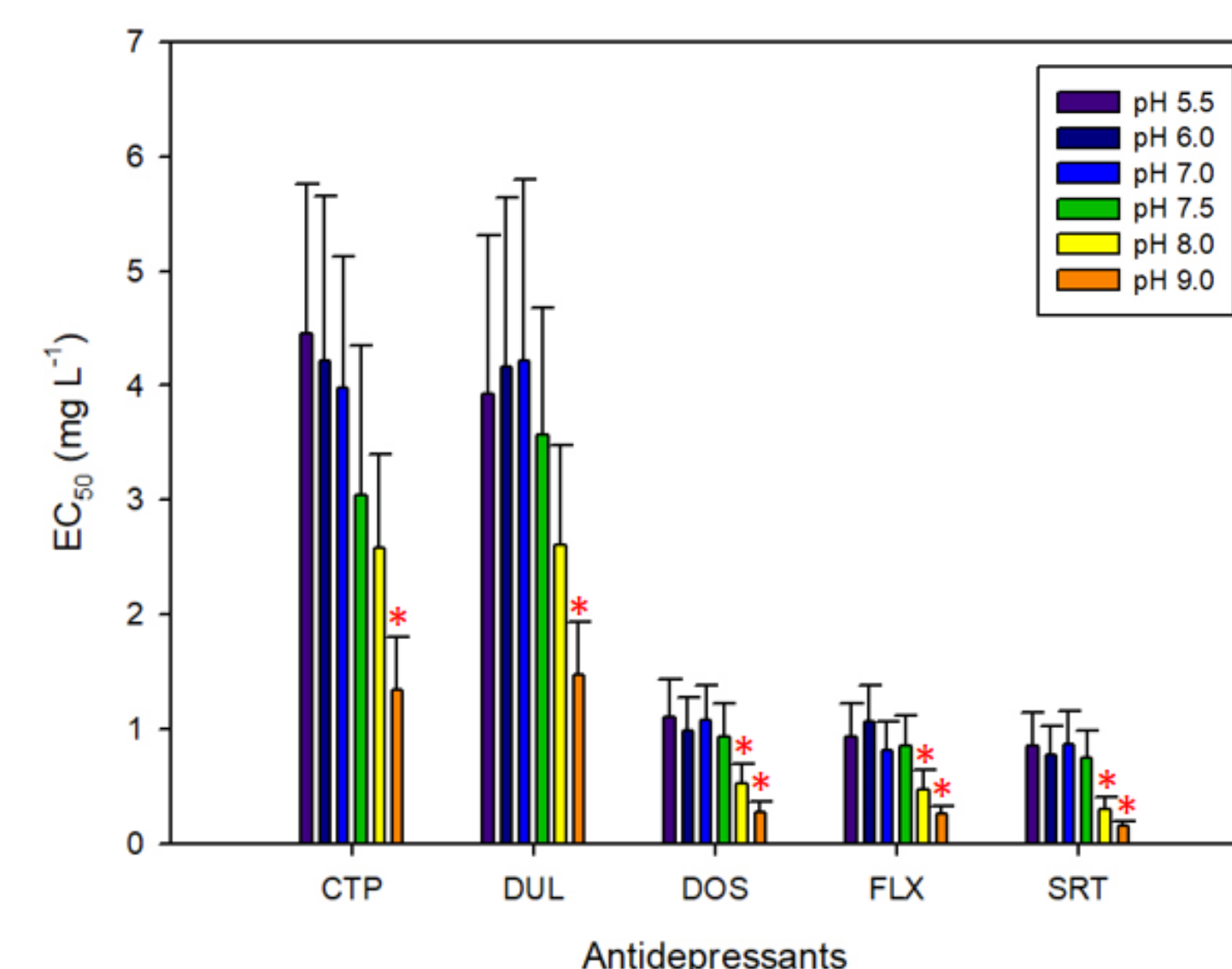


Figure 2. Decreased EC50 of *D. magna* with increasing pH

3. 21d *D. magna* chronic tests

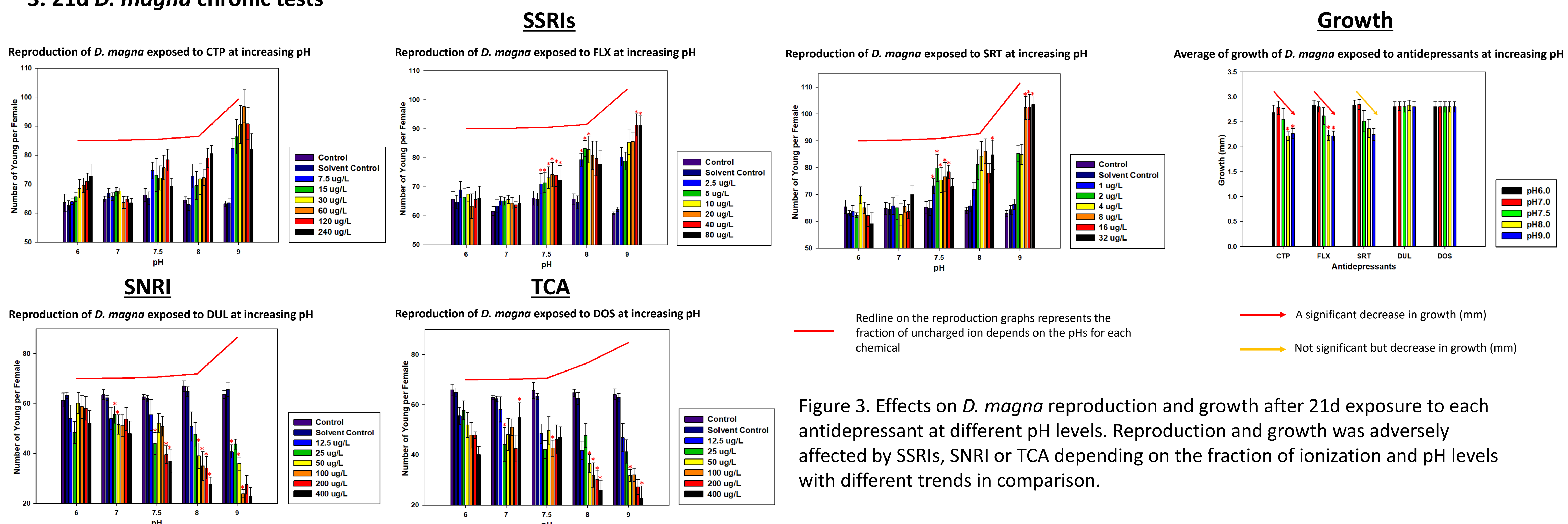


Figure 3. Effects on *D. magna* reproduction and growth after 21d exposure to each antidepressant at different pH levels. Reproduction and growth was adversely affected by SSRIs, SNRI or TCA depending on the fraction of ionization and pH levels with different trends in comparison.

Discussion & Conclusion

- The acute and chronic effects of each antidepressant increases with increasing pH levels.
- The greater proportion of the neutral species of each antidepressant corresponded with higher pH levels and likely explains the observed increase in the acute and chronic toxicity of antidepressants.
- A significantly greater reproduction but lower growth level was observed with SSRI chronic exposure. However, the SNRI and TCA have showed an opposite effect compared with SSRIs.
- Chronic tests for each antidepressant at pH 5.5 and mixture studies are still in progress which, when completed, will be used for parameterizing models to estimate the adverse effects of antidepressants to invertebrates in the surface water at wide range of pH values across the UK landscape.