

Table of contents

Preamble.....	3
1. General introduction	7
1.1. Essential oils and their main components.....	7
1.1.1. Carvacrol and thymol.....	9
1.1.2. Eugenol	12
1.1.3. Vanillin.....	14
1.2. Synthetic amorphous silica.....	17
1.2.1. Classification of silicon dioxide materials	17
1.2.2. Mesoporous silica: MCM-41 materials.....	20
1.2.3. Synthetic amorphous silica applications	20
1.2.4. Synthetic amorphous silica functionalisation.....	22
1.2.5. Toxicological evaluation of synthetic amorphous silica as a food additive.....	25
1.3. Toxicological assessment for food-regulated products	27
1.3.1. Guidance for submission for food additive evaluations.....	28
1.3.2. Guidance on risk assessment of applying nanoscience and nanotechnologies in the food and feed chain	29
1.3.3. Guidelines indicating the necessary documentation for assessing the processing aids intended for use in human food.....	32
1.4. The 3Rs strategy for toxicity testing.....	35
2. Objectives.....	39
3. Experimental outline	43
4. Chapter 1. Stability in physiological fluids.....	47
4.1. Degradation of silica particles functionalised with essential oil components under simulated physiological conditions.....	53
5. Chapter 2. <i>In vitro</i> toxicity study	93
5.1. Comparative cytotoxic study of silica materials functionalised with essential oil components in HepG2 cells.	101

5.2. <i>In vitro</i> toxicological evaluation of mesoporous silica microparticles functionalised with carvacrol and thymol.....	142
6. Chapter 3. <i>In vivo</i> toxicity study	191
6.1. Effects of essential oil components exposure on biological parameters of <i>Caenorhabditis elegans</i>	201
6.2. <i>In vivo</i> toxicity assessment of eugenol and vanillin-functionalised silica particles using <i>Caenorhabditis elegans</i>	243
7. General discussion	285
8. Conclusions	297
References	301