Oxidative Degradation of SSRIs by Fe^{III}–TAML/H_2O_2 Activators

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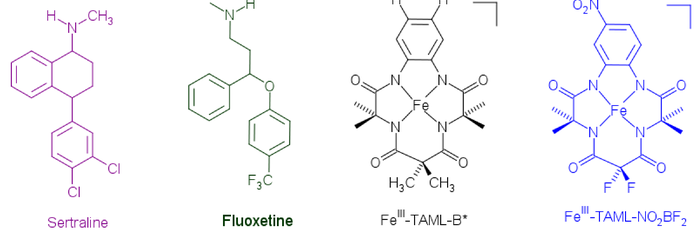
Background

❖ Pharmaceuticals are designed to resist degradation to maximize their effectiveness. As a result, they can escape the degradation processes of the body and waste treatment plants and end up in environmental waters where they can cause harm to aquatic life forms. Pharmaceuticals and their active metabolites are known to be prevalent in environmental waters and are high profile environmental pollutants.[1,2]

❖ Zoloft® (sertraline) and Prozac® (fluoxetine) are from the group of selective serotonin reuptake inhibitors (SSRI), which are widely prescribed to alleviate depression syndromes. Both sertraline and fluoxetine have been identified in environmental waters and are associated with adverse effects on aquatic organisms.[3,4,5]

❖ Fe^{III}–TAMLs (Tetra-Amido Macrocyclic Ligands) are a family of green oxidation catalysts that mimic peroxidase function. The system efficiently degrades sertraline and fluoxetine in water at pH 9.5 under ambient conditions resulting in the major metabolites of cytochrome P450 degradation along with additional oxidative species.[6,7]

Structures



Instrumentation

Liquid chromatography (LC) was completed with a Waters 600E series LC or a Michrom BioResources MAGIC 2002 LC. Flow injection and LC coupled mass spectrometry (MS) were carried out on a Thermo LCQ™ 3D Ion Trap equipped with electrospray (ESI) and atmospheric pressure chemical ionization (APCI) sources. Gas chromatography (GC) coupled MS was completed on a Thermo DSQ™ mass spectrometer with a TRACE GC equipped with a Programmed Temperature Vaporizing (PTV) injector. Solid phase extraction (SPE) was done with Waters Oasis® HLB cartridges and solid phase microextration (SPME) was done using a PDMS fiber from Supelco.® LC separation was done on a Waters Xterra® C18 column (150 mm, 4.6 mm id, 5 µM particles) and GC separation was done using a Restek Rtx® -XLB column (30 m, 0.25 mm id, 0.25 µM film)

Acknowledgement

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References

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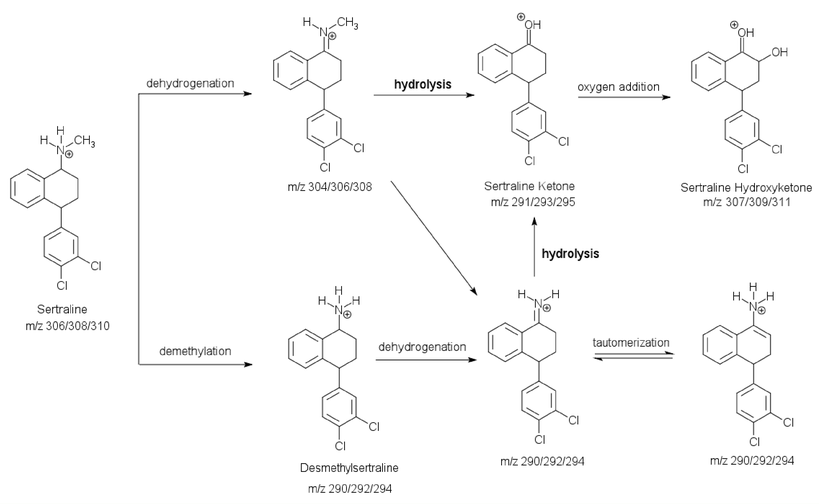
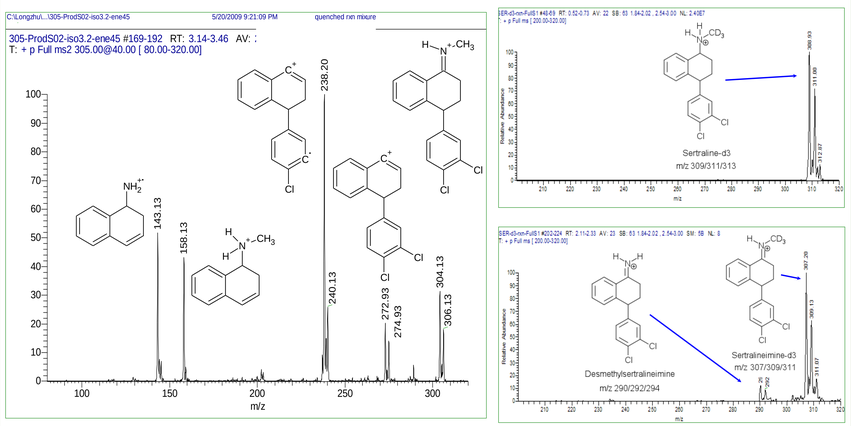
Sertraline

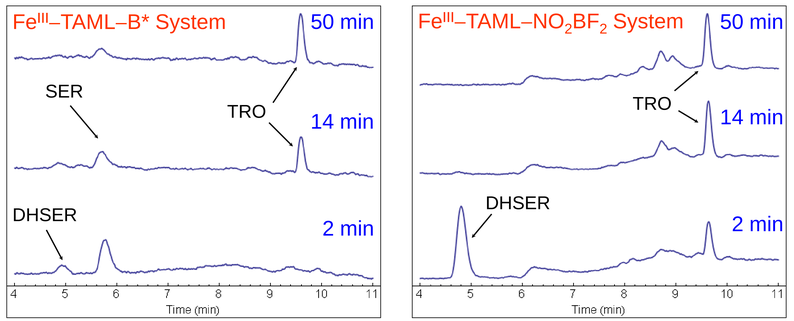
Predicted reaction pathway for sertraline degradation by Fe^{III}–TAML/H_2O_2



Dehydrogenation products of sertraline and sertraline-*d3* by APCI-MS



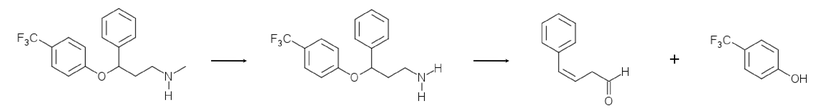
Comparison of reaction rates for two TAML systems by LC monitoring



DHSER = dehydrogenated sertraline, SER = sertraline, TRO = sertraline ketone

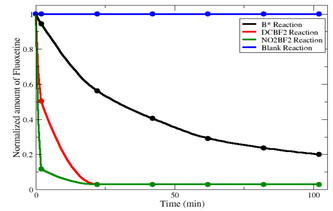
Fluoxetine

Predicted reaction pathway for fluoxetine degradation by Fe^{III}–TAML/H_2O_2

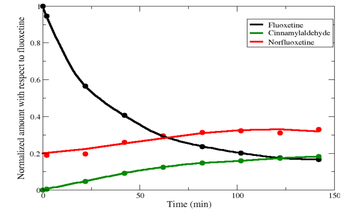


fluoxetine → norfluoxetine → cinnamylaldehyde + trifluoro-*p*-cresol

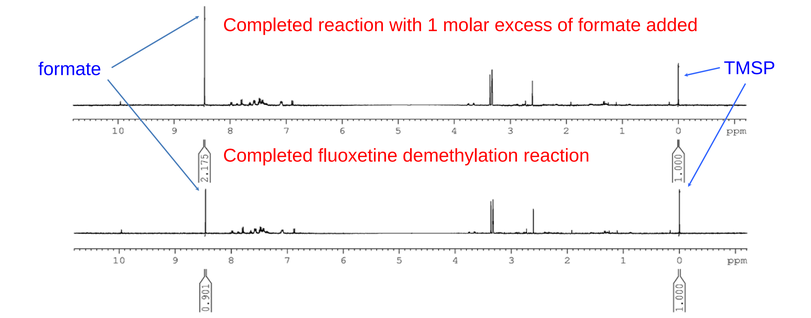
Fluoxetine decay curve with different Fe^{III}–TAML activators



Time evolution of fluoxetine reaction species with Fe^{III}–TAML–B*



Fate of fluoxetine methyl group after demethylation step characterized by NMR



Fluoxetine degradation products characterized by SPME GC-MS