On the Oxidative Degradation of Sertraline by the Catalytic Fe^{III}–TAML/H_2O_2 System followed by Chromatography/Tandem Mass Spectrometry

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OVERVIEW

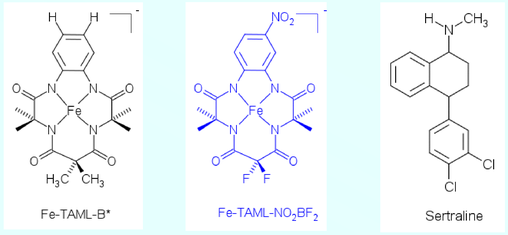
- Monitor oxidative transformation process of sertraline by Fe^{III}-TAML/H_2O_2 system
- Identify the oxidation products by chromatography/tandem mass spectrometry
- Probe the oxidation mechanism through product characterization

INTRODUCTION

- Pharmaceuticals are designed to resist degradation to maximize their effectiveness. As a result, they escape the degradation processes of the body and treatment plants to end up in environmental waters where they can harm aquatic organisms.
- Pharmaceuticals and their active metabolites are now known to be prevalent in water and are high profile environmental pollutants.
- Zoloft® (sertraline) is a selective serotonin reuptake inhibitor (SSRI), which is widely prescribed to alleviate depression syndromes. Sertraline has been identified in environmental waters and is associated with adverse effects on aquatic organisms.
- The Fe^{III}-TAML/H_2O_2 has been shown through mechanistic and applications studies to be an outstanding peroxidase enzyme mimic. Here we show that the system efficiently degrades sertraline in water at pH 9.5 under ambient conditions passing through the major metabolites of cytochrome P450 degradation and additional species.

METHODS

Materials



Reaction Conditions

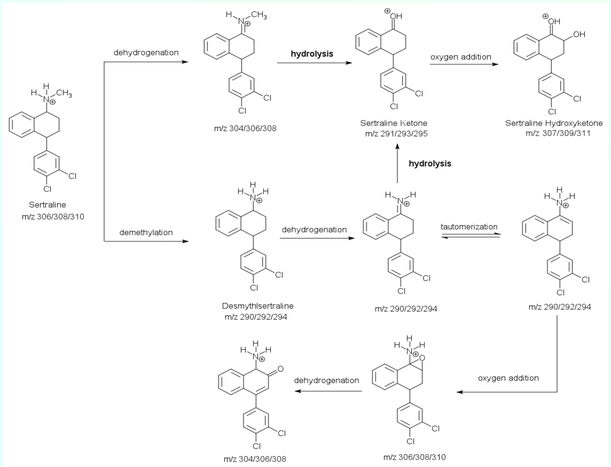
The Fe^{III}–TAML/H_2O_2 catalyzed transformation of sertraline (10 μM) was performed in $NaHCO_3$/Na_2CO_3 buffer (5 mM, pH 9.5) around a molar Fe^{III}–TAML:sertraline:H_2O_2 ratio of 0.5:100:3650. A series of Fe^{III}–TAML catalysts were utilized to characterize the effects of using catalysts of different oxidative aggressiveness and pH of maximum activity.

Instrumentation

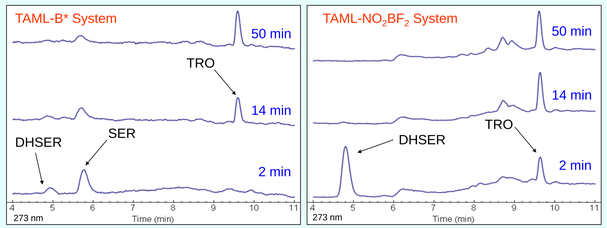
Liquid chromatography was performed with a Waters 600E series LC or a Michrom BioResources Magic 2002 LC. Capillary LC was carried out on a home-made C18 capillary column. Flow injection and LC coupled mass spectrometric analyses were carried on a Thermo Fisher LCQ 3D Ion Trap equipped with ESI and APCI sources. Gas chromatography coupled mass spectrometry was performed on a Thermo Scientific DSQ mass spectrometer with a TRACE GC system.

RESULTS

Proposed oxidative transformation pathway of sertraline



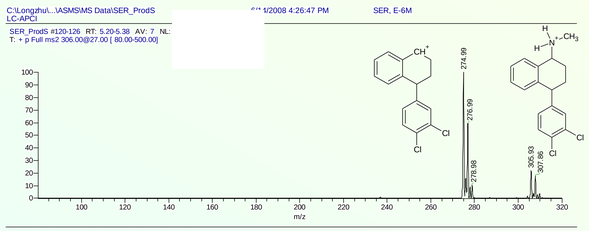
Oxidation Efficiency Comparison by HPLC

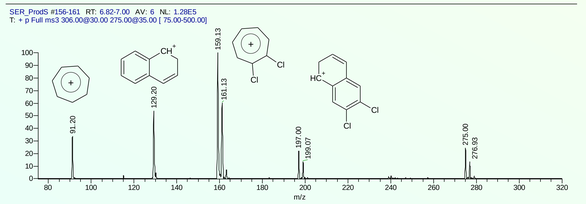


DHSER = dehydrogenated sertraline, SER = sertraline, TRO = sertraline ketone

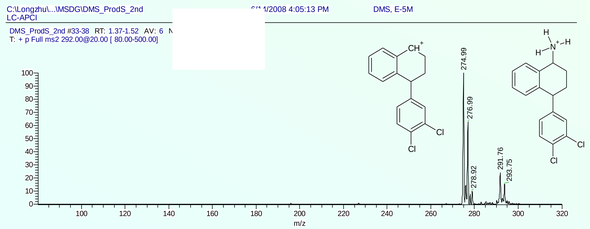
Reaction Products Identification — APCI-MS Product Scan

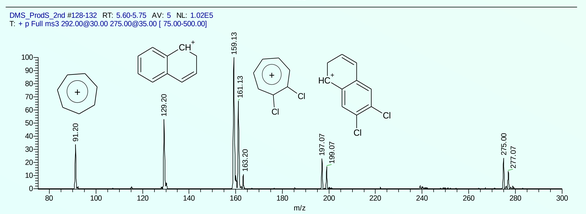
♣ Sertraline Standard



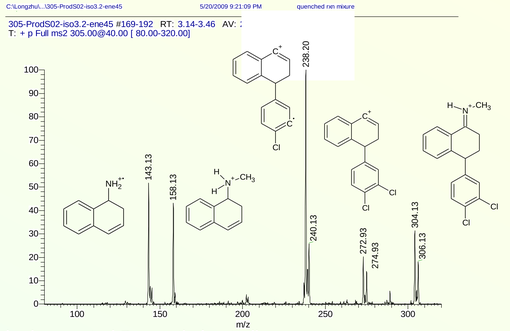


♣ N-Desmethylsertraline

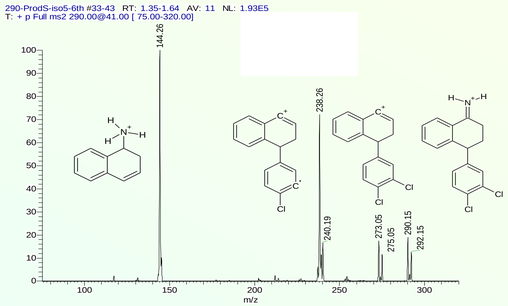




♣ Dehydrogenated Sertraline



♣ Dehydrogenated Desmethylsertraline



Sertraline demethylation and deamination products were also confirmed by GC/MS experiments. A product tentatively assigned to be sertraline hydroxyketone was detected by capillary-LC-MS.

CONCLUSIONS

This study has shown that Fe^{III}–TAML can mimic cytochrome P450 to oxidize sertraline by going through all major metabolites. However, the dehydrogenation products of sertraline and desmethylsertraline have not been reported in enzymatic studies. The oxidative transformation pathway of sertraline is proposed based on reaction products characterization by chromatography hyphened mass spectrometry.

ACKNOWLEDGEMENT

Special thanks to Evan Beach for synthesizing sertraline and its metabolites.