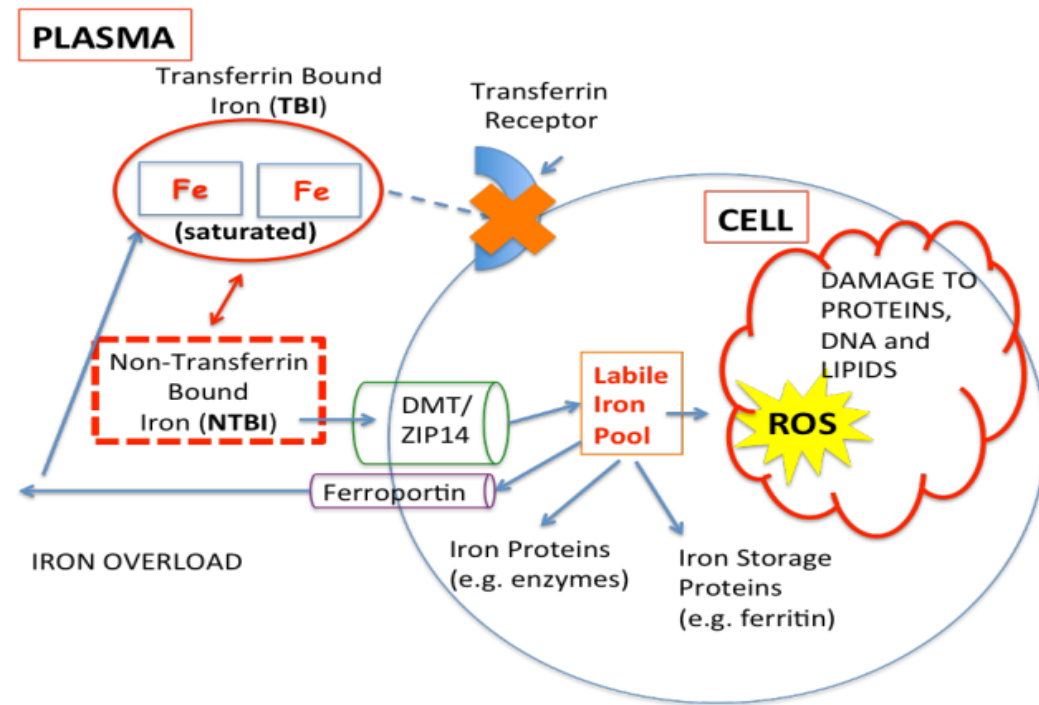


# **EVALUATION OF BIOMARKERS IN HEALTHY SUBJECTS TREATED WITH GENERIC AND REFERENCE SODIUM FERRIC GLUCONATE**

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# Introduction

- Normally, >95% of iron in the body is protein bound and the major form of non-heme iron in plasma is transferrin-bound iron (TBI).
- When the normal occupancy of serum transferrin is exceeded iron overload can occur.
- The resulting “free” pool of iron that is bound to ligands other than transferrin (non-transferrin bound iron, NTBI) is increased.
- Excess labile iron can lead to the generation of reactive oxygen species (ROS) and oxidative stress, lipid peroxidation, DNA damage, and inflammation.

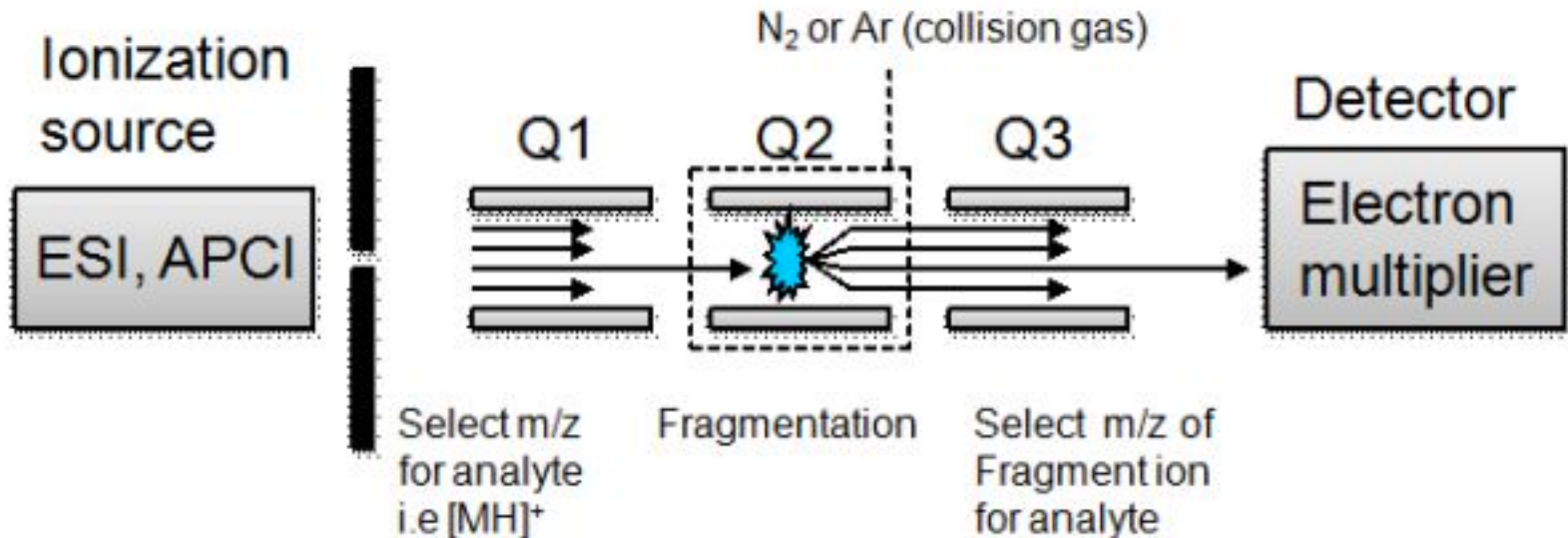


# Lipid Peroxidation

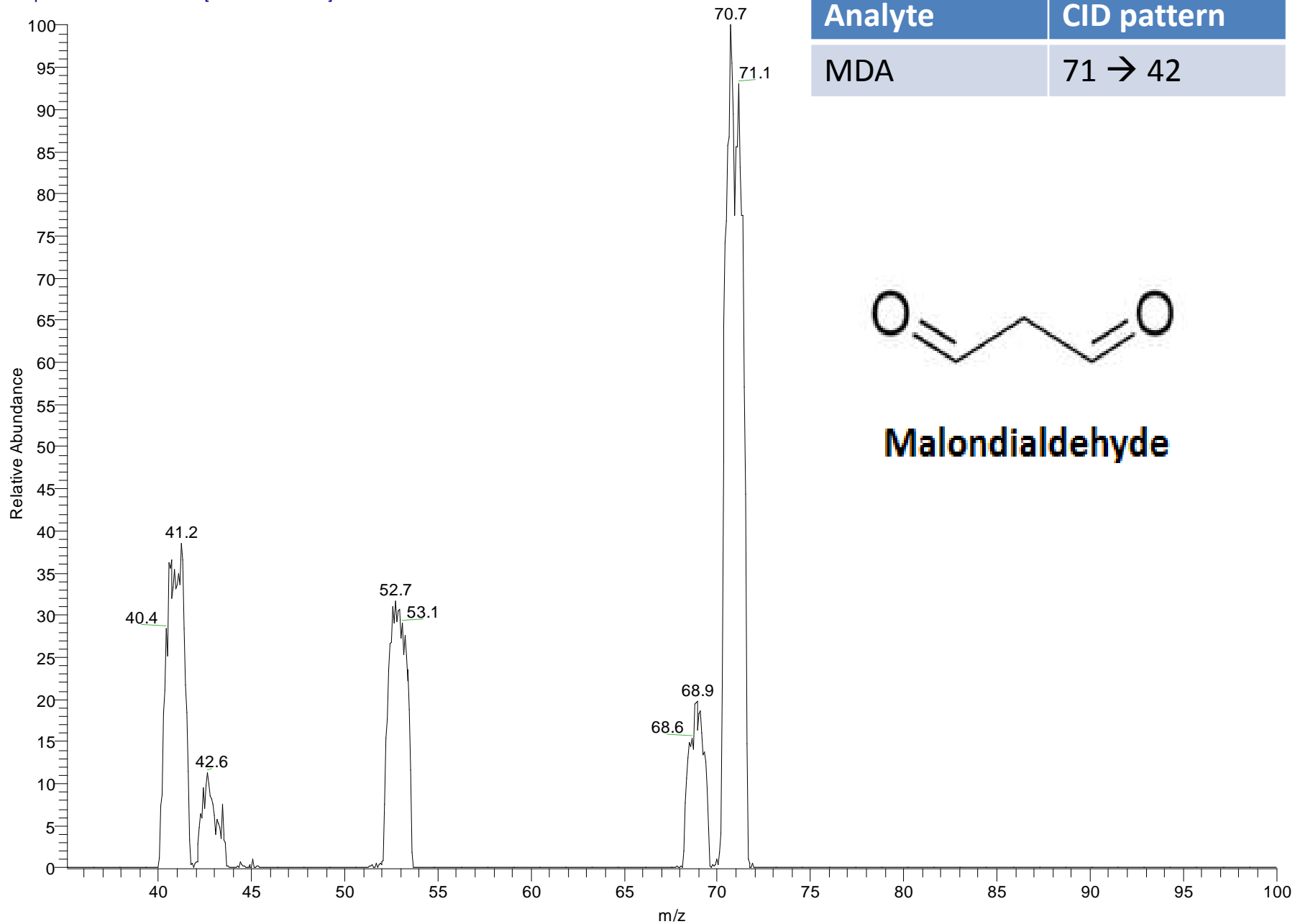
- The main targets of free radicals are lipids where free radical attack results in lipid peroxidation.
- Malondialdehyde (MDA) is one of the final products of polyunsaturated fatty acid peroxidation in cells.
- An increase in free radicals causes overproduction of MDA.
- MDA will be quantified in patient plasma after RLD or generic sodium ferric gluconate product treatment at time 0, 6h, 24h, and 36h after dose.
- An **elevation in MDA will indicate greater oxidative stress.**

# Methodology

- MDA will be quantified by LC-MS/MS and monitored by MRM
- MDA standard will be obtained by acid hydrolysis
- MeMDA will be used as internal standard



MDA-100uM\_MS2 #3-29 RT: 0.04-0.48 AV: 27 NL: 4.39E4  
T: - p ESI Full ms2 71.054 [35.070-100.000]



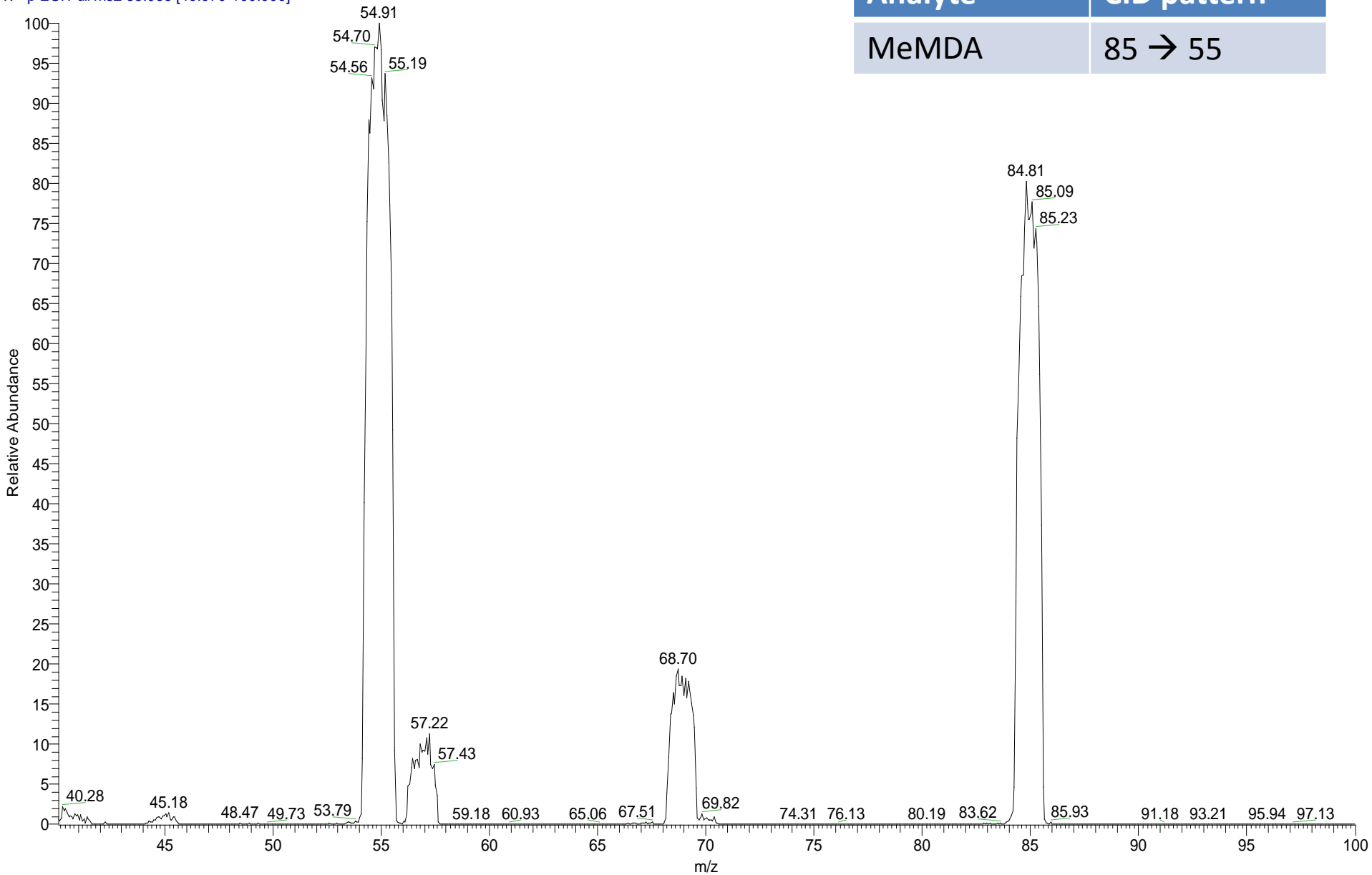
MDA

Analyte	CID pattern
MDA	71 → 42



**Malondialdehyde**

Me-MDA10um\_MS2 85\_001 #5-113 RT: 0.04-0.96 AV: 109 NL: 3.41E4  
T: -p ESI Full ms2 85.065 [40.070-100.000]



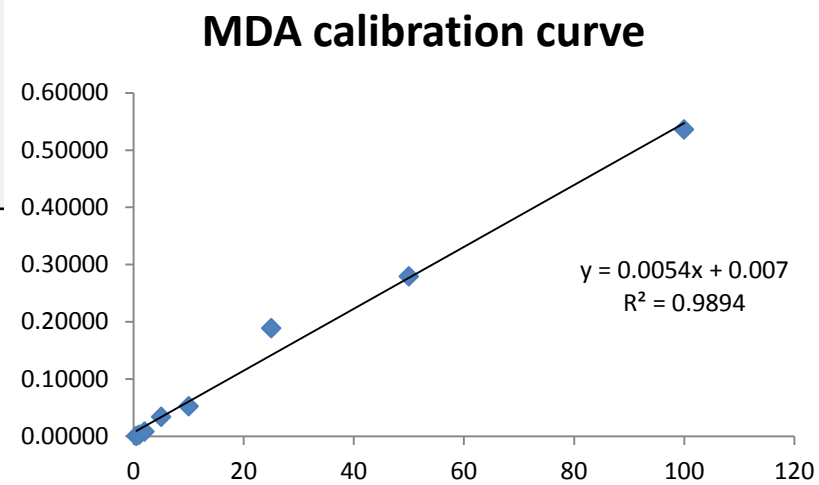
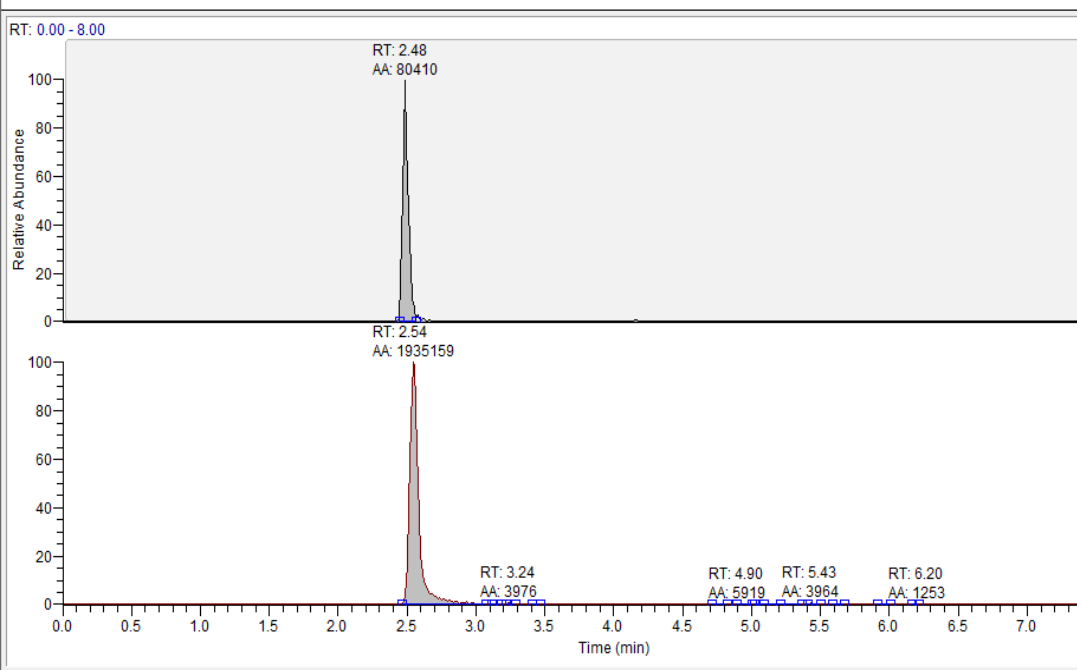
Analyte

MeMDA

CID pattern

85 → 55

# MRM Chromatogram for MDA and MeMDA (internal standard)



# Conclusion

- Quantification of MDA will determine if generic sodium ferric gluconate can cause lipid peroxidation
- By doing so, we can assess any concern of iron impurities in generic formulations