

PHARMACEUTICAL IMPURITY PROFILING METOCLOPRAMIDE IMPURITIES

In the modern pharmaceutical industry, it is critically important to identify and quantify impurities with the highest possible confidence given their potential toxic effects on humans. This report describes the performance of the Agilent 6545 Q-TOF LC/MS system in the determination of metoclopramide pharmaceutical impurities.

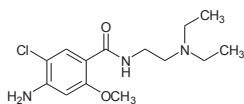
In this, the 6545 Q-TOF and 1290 Infinity LC system are used to determine metoclopramide impurities (structures below).

Metoclopramide standard prepared at 500 ppm was spiked with all known impurities described in European Pharmacopoeia and two additional impurities at 0.05% (w/w) and 0.01% (w/w) levels.

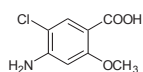
Enormous gain in sensitivity supports identification of impurities

The improved sensitivity of the 6545 Q-TOF LC/MS enables identification of the profiled pharmaceutical impurities at both 0.05% and 0.01% spiked

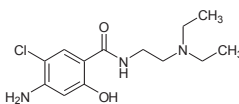
levels in the presence of saturating active pharmaceutical ingredient, metoclopramide. Mass accuracies are typically below 1 ppm. An improvement in MS detection response of 4 to 13-fold is achieved compared with previous generation Q-TOF LC/MS (see table on back). Simultaneously acquired UV data indicates that the sensitivity gain originates solely from the performance of the MS system. Impurity H could only be detected on the 6545 Q-TOF.



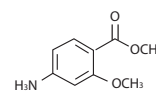
Metoclopramide



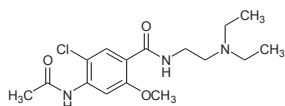
Impurity C



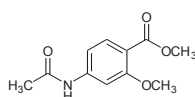
Impurity F



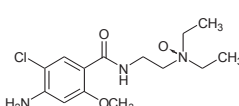
Impurity I



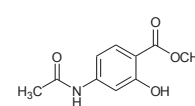
Impurity A



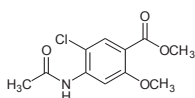
Impurity D



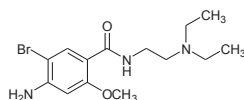
Impurity G



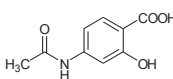
Impurity J



Impurity B



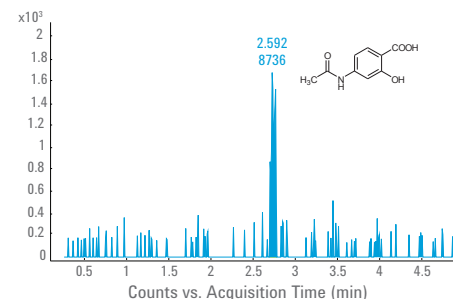
Bromated Metoclopramide



Impurity H



Impurity	UV area 6545	UV area previous generation Q-TOF	UV area 6545/UV area previous generation Q-TOF	MS area 6545	MS area previous generation Q-TOF	MS area 6545/MS area previous generation Q-TOF
Imp C	0.79	0.82	0.96	59847	5572	10.74
Imp H	1.82	1.75	1.04	8736	ND	∞
Imp G	1.74	1.66	1.05	19802772	1528522	12.96
Imp F	2.23	2.13	1.05	24918063	2072689	12.02
Imp A	1.21	1.17	1.03	15995304	1492777	10.72
Metoclopramide	4132.46	4133.52	1.00	Saturated	Saturated	-
Br metoclopramide	5.04	5.48	0.92	48747844	4853213	10.04
Imp D	2.52	2.32	1.09	187965	24010	7.83
Imp J	3.09	3.17	0.97	29878	7372	4.05
Imp I	2.63	2.84	0.93	ND	ND	-
Imp B	1.33	1.26	1.06	42134	7477	5.64



0.05% Impurity H can be detected only by 6545 Q-TOF.

The 6545 Q-TOF LC/MS also enables structure confirmation by MS/MS fragmentation using library search or Molecular Structure Correlator (MSC) with ChemSpider. Here, collision energies of 10, 20 and 40 eV are applied. METLIN and the Toxicology/Forensic library enable identification of metoclopramide and bromated metoclopramide. MSC with ChemSpider are used to identify the remaining impurities.

"The 6545 Q-TOF offers a substantial leap forward in sensitivity while maintaining all other features one expects from a high-end Q-TOF system. Together with the improved robustness and advanced-yet-user-friendly tuning, the 6545 Q-TOF can be a workhorse in both targeted and untargeted profiling of small molecules in a wide range of applications."

— Dr. Koen Sandra, director of R&D, Research Institute of Chromatography

The 6545 Q-TOF has enabled us to detect impurities and confirm their structure in pharmaceutical samples that we may have overlooked in previous efforts.

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Published in the USA, May 19, 2015
5991-5878EN

