Table 1: Comparison between our current manuscript with previous literature dealing with the analysis of LND and DEX in biological fluids.

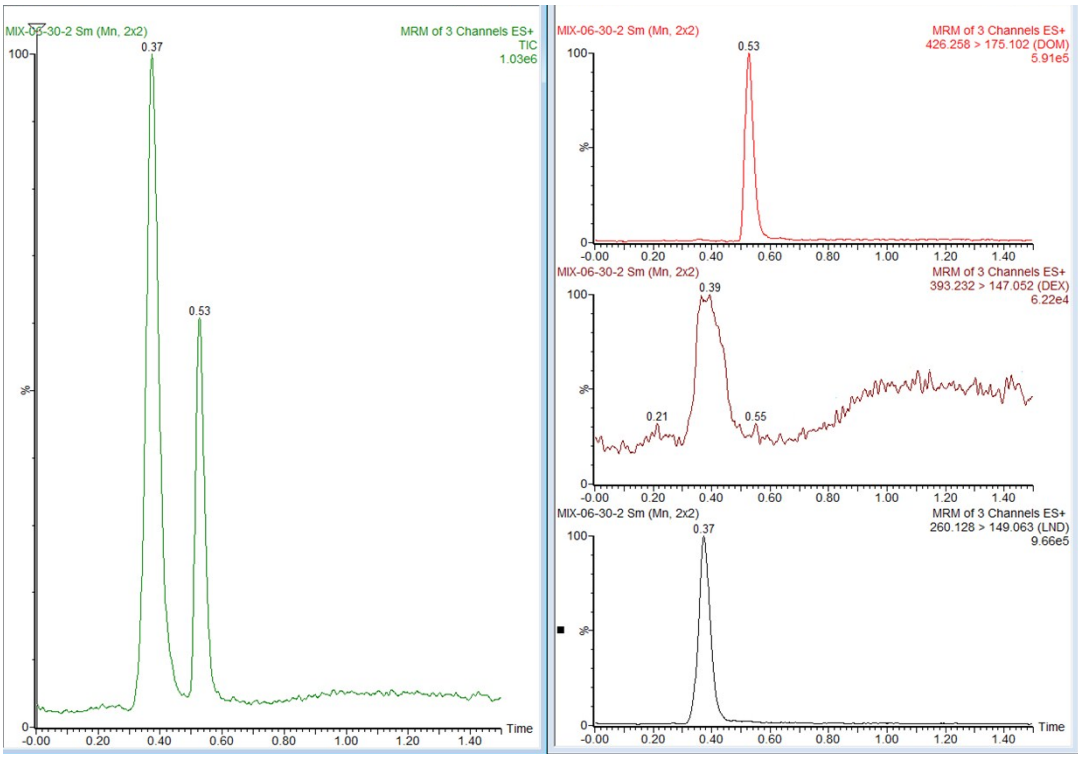
Analytical method [Reference number]	Linearity range	LOD	LOQ	Application	Remarks
LND					
HPLC-UV					
[26]	0.1-50 nM	0.009 nM	0.1 nM	Determination of LND in human plasma and cerebrospinal fluid	*SPE of the analyzed samples. *Total run time was 7 min. LND was eluted at 5.5 min.
HPLC-fluorimetry					
[27]	5-100 ng/mL	0.8 ng/mL	2.3 ng/mL	Determination of LND in spiked plasma samples.	*Protein precipitation of the analyzed samples with acetonitrile followed by complexation of the endogenous amino acids with copper ions. *Precolumn derivatization with fluorescamine. *Total arun time was 20 min. LND was eluted at 11.6 min.
HPLC-MS					
[28]	The same analytical method as reference [24]			Estimation of the maximum tolerated dose (MTD), describes toxicities, and evaluates pharmacokinetics.	*SPE of blood samples
[29]	5-100 ng/mL	Not mentioned	5 ng/mL	-Quantitation of LND in human plasma. -Application to a pharmacokinetic study in a single patient.	*LLE of the plasma sampls with acetonitrile/1-chlorobutane (4:1, v/v). * Total run time was 8 min. LND was eluted at 3.2 min.
LC-MS/MS					
[30]	2-1000 ng/mL	Not mentioned	2 ng/mL	-Quantitation of LND in human plasma	*SPE of plasma samples. *Box-Behnken experimental design was applied for the validation of robustness. * Total run time was

					3 min. LND was eluted at 1.04 min.
[31]	0.97-486.19 ng/mL	Not mentioned	0.97 ng/mL	-Simultaneous quantitation of LND, idelalisib, and fudarabine in rat plasma. -Application to a pharmacokinetic study.	*LLE of plasma samples with t-butyl methyl ether. * Total run time was 4 min. LND was eluted at 3.0 min
[32]	5-1000 ng/mL	Not mentioned	5 ng/mL	-Assessment of the pharmacokinetics of [^{14}C] LND following oral administration in healthy human subjects. -Application to plasma, feces, urine, and semen samples.	* All samples required pH adjustment before analysis. *The use of radio-scintillation counter for measuring the radioactivity. * Total run time was 50 min. LND was eluted at 30.1 min
[33]	1-1000 nM	Not mentioned	1 nM	-Simultaneous quantitation of LND and flavopiridol in human plasma.	* LLE of plasma samples. * Total run time was 10 min. LND was eluted at 1.04 min.
UPLC-MS/MS					
[34]	0.23-1000 ng/mL	Not mentioned	0.23 ng/mL	-Determination of LND in spiked animal and human plasma samples.	*Protein precipitation of plasma samples with methanol. * Total run time was 3 min. LND was eluted at 0.70 min.
Current method	0.01-0.5 ng/mL	0.004 ng/mL	0.01 ng/mL	-Determination of LND and DEX in plasma samples. -Determination of the pharmacokinetics of LND either alone or in combination with LND following oral administration to rats.	*SPE of the analyzed sample. * Total run time was 1.5 min. LND was eluted at 0.36 min.
DEX					
HPLC-UV					
[35]	0.702-70.2 ng/mL	Not mentioned	0.702 ng/mL	-Evaluation of the pharmacodynamics, pharmacokinetics, and comparative bioavailability of a commercial oral	*LLE of plasma samples with diethylether. * Total run time was 25.5 min.

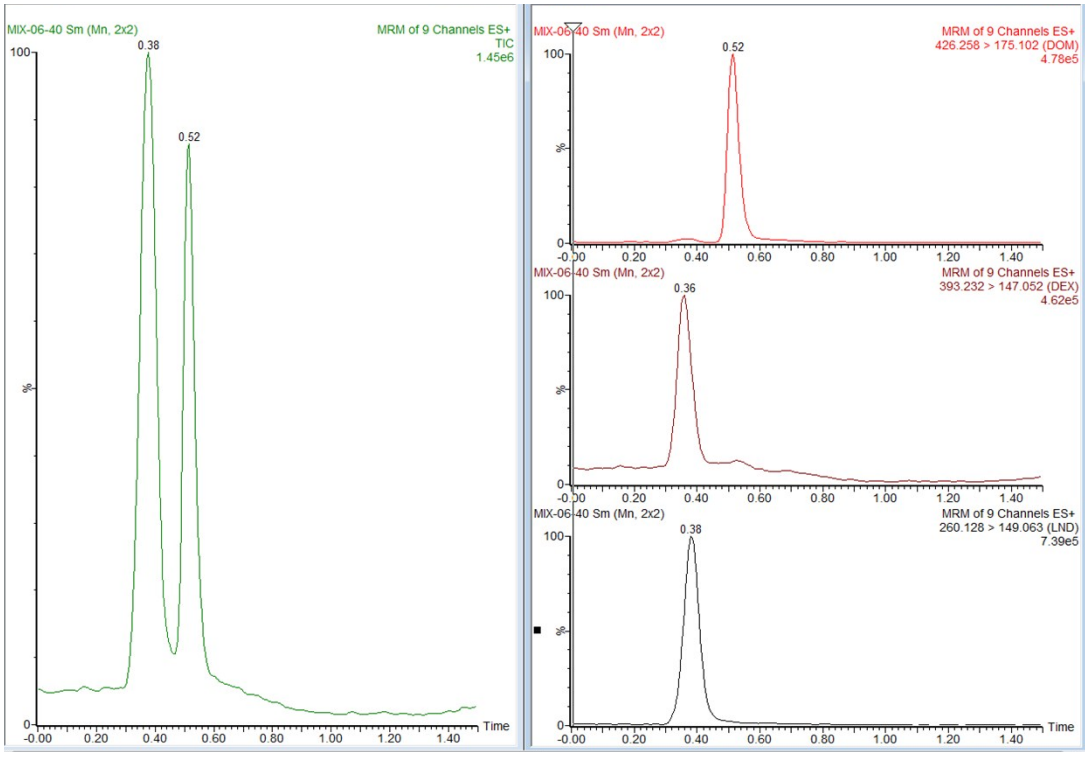
				DEX formulation intended for pediatric use relative to those in tablets. -Determination of DEX in human plasma.	
LC-MS					
[36]	6-100 ng/mL	1 ng/mL	6 ng/mL	-Determination of DEX in sheep plasma. -Application to a pharmacokinetic study.	* SPE of plasma samples. *Total run time was 9 min. DEX was eluted at 5.83 min.
[37]	4.5-450 pmol	1 pmol	4.5 pmol	-Quantitation of DEX in blood samples.	*LLE of plasma samples with diethylether. *Total run time was 10 min. DEX was eluted at 5.0 min.
LC-MS/MS					
[38]	2.5-250 ng/mL	0.6 ng/mL	2.5 ng/mL	-Simultaneous determination of DEX and DEX palmitate in human plasma. -Application to a pharmacokinetic study following IV injection to human volunteers.	*LLE of plasma samples with diethylether : dichloromethane (60:40, v/v). * Total run time was 6 min. DEX was eluted at 4.2 min.
[39]	0.5-500 µg/L	Not mentioned	0.5 µg/L	-Determination of DEX and DEX sodium palmitate in plasma and human cochlear perilymph. -Application to a pharmacokinetic study.	*Protein precipitation of the analyzed samples with methanol/acetonitrile (1: 4, v/v). * Total run time was 5 min. DEX was eluted at 2.79 min.
[40]	2-1000 ng/mL	0.01 ng/mL	2 ng/mL	-Determination of the pharmacokinetics of DEX in broiler chicken. -Quantitation of DEX in plasma samples.	*Protein precipitation of the analyzed samples with 20% trichloroacetic acid followed by LLE with diethyl ether. *Total run time was 6 min.
UPLC-MS					
[41]	1-5 µg/L	0.1 µg/L	0.6 µg/L	-Multidetection of corticosteroids in sports doping and	*LLE of the analyzed samples with diethylether.

				veterinary control. -Multiresidue analysis of corticosteroids in human and veterinary urine.	*Total run time was 7.5 min. DEX was eluted at 3.6 min.
UPLC-MS/MS					
[42]	5-500nmol/L	Not mentioned	1 nmol/L	-Determination of corticosteroid mixtures in plasma, urine, and saliva.	*SPE of the analyzed sample. * Total run time was 3 min. DEX was eluted at 2.02 min.
Current method	0.01-0.5 ng/mL	0.004 ng/mL	0.01 ng/mL	-Determination of LND and DEX in plasma samples. -Determination of the pharmacokinetics of DEX either alone or in combination with LND following oral administration to rats.	*SPE of the analyzed sample. * Total run time was 1.5 min. DEX was eluted at 0.36 min.

a)


MIX-06-30-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
TIC
1.03e6
0.37
0.53
MIX-06-30-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
426.258 > 175.102 (DOM)
5.91e5
0.53
MIX-06-30-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
393.232 > 147.052 (DEX)
6.22e4
0.39
0.21
0.55
MIX-06-30-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
260.128 > 149.063 (LND)
9.66e5
0.37
%
Time

b)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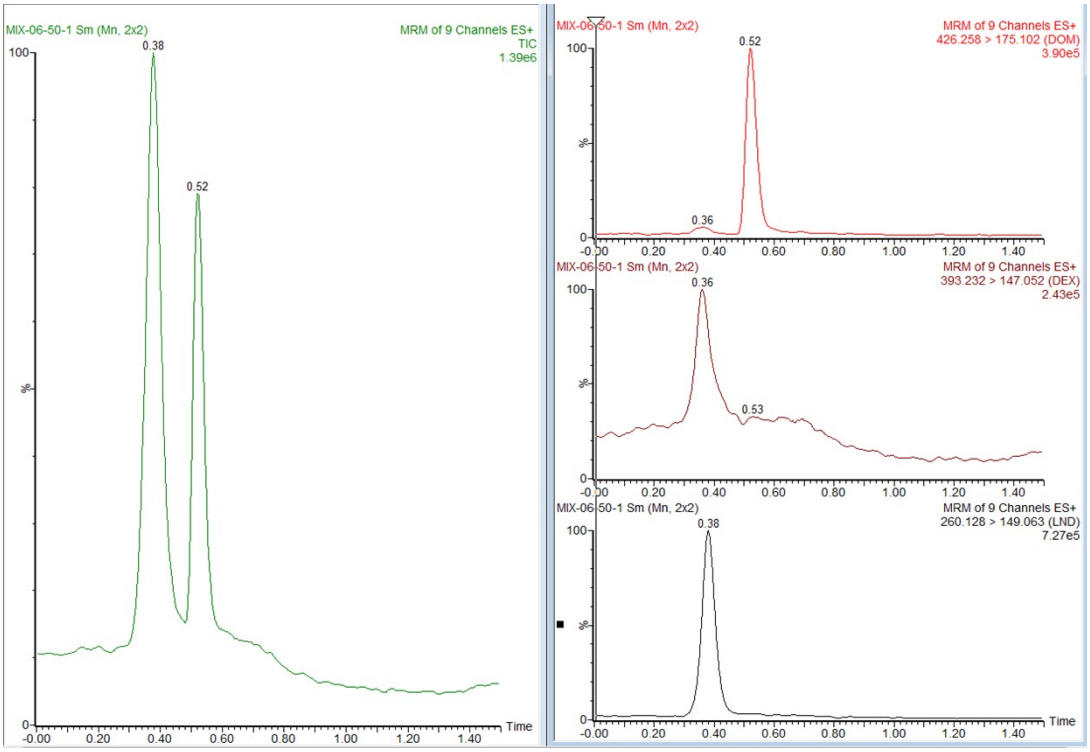
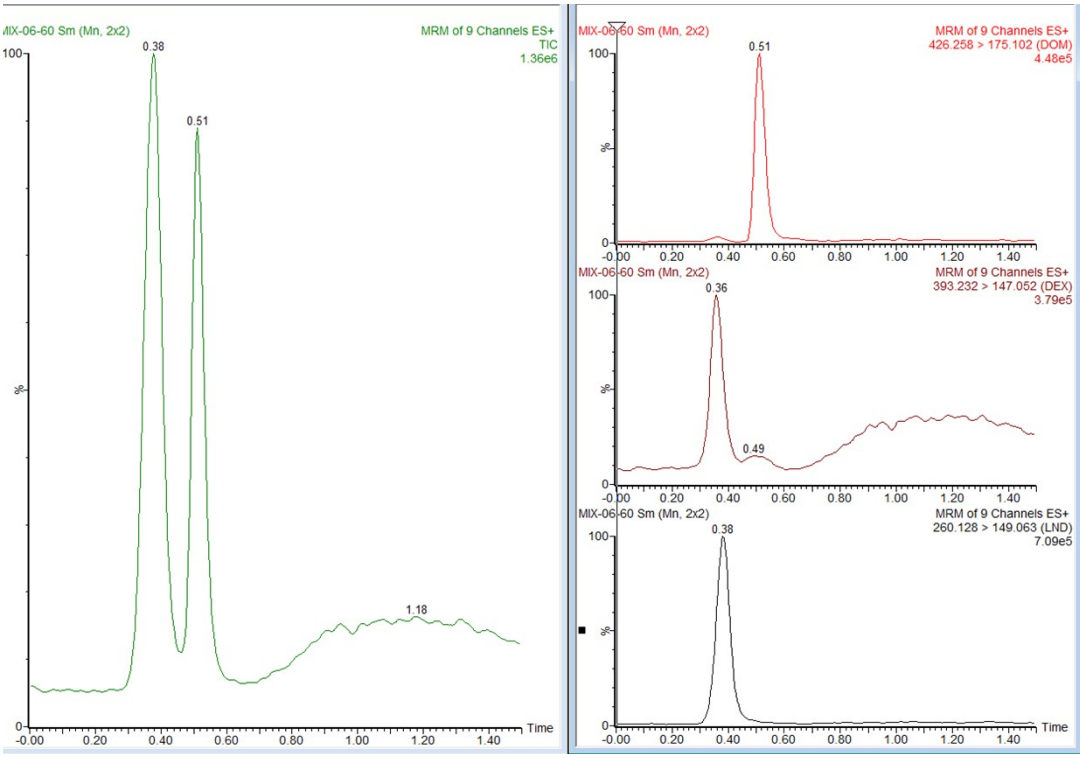
MRM of 9 Channels ES+
TIC
1.45e6
0.38
0.52
MIX-06-40 Sm (Mn, 2x2)
MRM of 9 Channels ES+
426.258 > 175.102 (DOM)
4.78e5
0.52
MIX-06-40 Sm (Mn, 2x2)
MRM of 9 Channels ES+
393.232 > 147.052 (DEX)
4.62e5
0.36
MIX-06-40 Sm (Mn, 2x2)
MRM of 9 Channels ES+
260.128 > 149.063 (LND)
7.39e5
0.38
%
Time

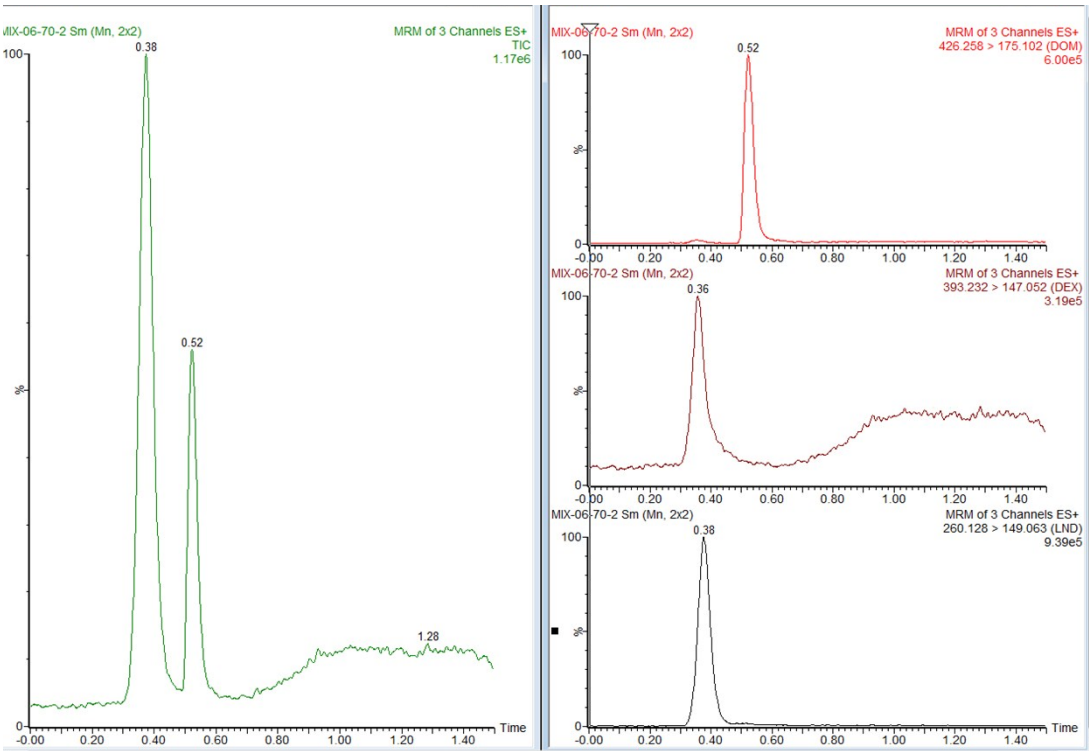
c)


MIX-06-50-1 Sm (Mn, 2x2)
MRM of 9 Channels ES+
TIC
1.39e6
0.38
0.52
MIX-06-50-1 Sm (Mn, 2x2)
MRM of 9 Channels ES+
426.258 > 175.102 (DOM)
3.90e5
0.52
0.36
MIX-06-50-1 Sm (Mn, 2x2)
MRM of 9 Channels ES+
393.232 > 147.052 (DEX)
2.43e5
0.36
0.53
MIX-06-50-1 Sm (Mn, 2x2)
MRM of 9 Channels ES+
260.128 > 149.063 (LND)
7.27e5
0.38
%
Time

d)


MIX-06-60 Sm (Mn, 2x2)
MRM of 9 Channels ES+
TIC
1.36e6
0.38
0.51
1.18
MIX-06-60 Sm (Mn, 2x2)
MRM of 9 Channels ES+
426.258 > 175.102 (DOM)
4.48e5
0.51
MIX-06-60 Sm (Mn, 2x2)
MRM of 9 Channels ES+
393.232 > 147.052 (DEX)
3.79e5
0.36
0.49
MIX-06-60 Sm (Mn, 2x2)
MRM of 9 Channels ES+
260.128 > 149.063 (LND)
7.09e5
0.38
%
Time

e)



f)

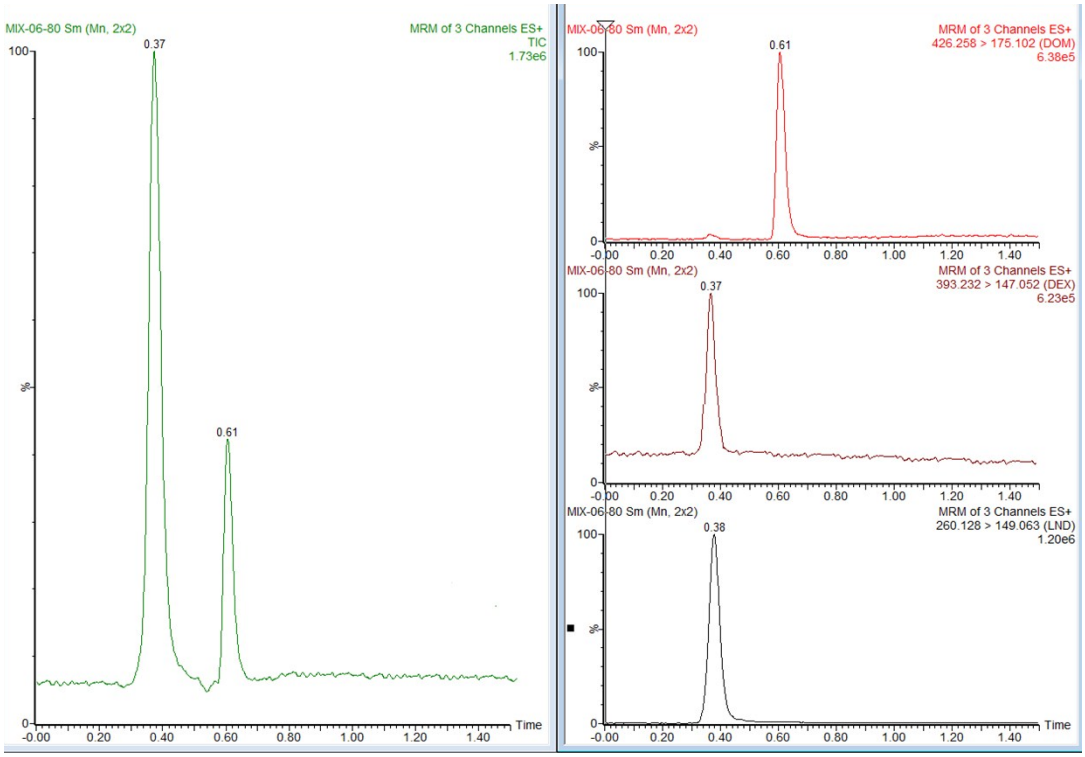
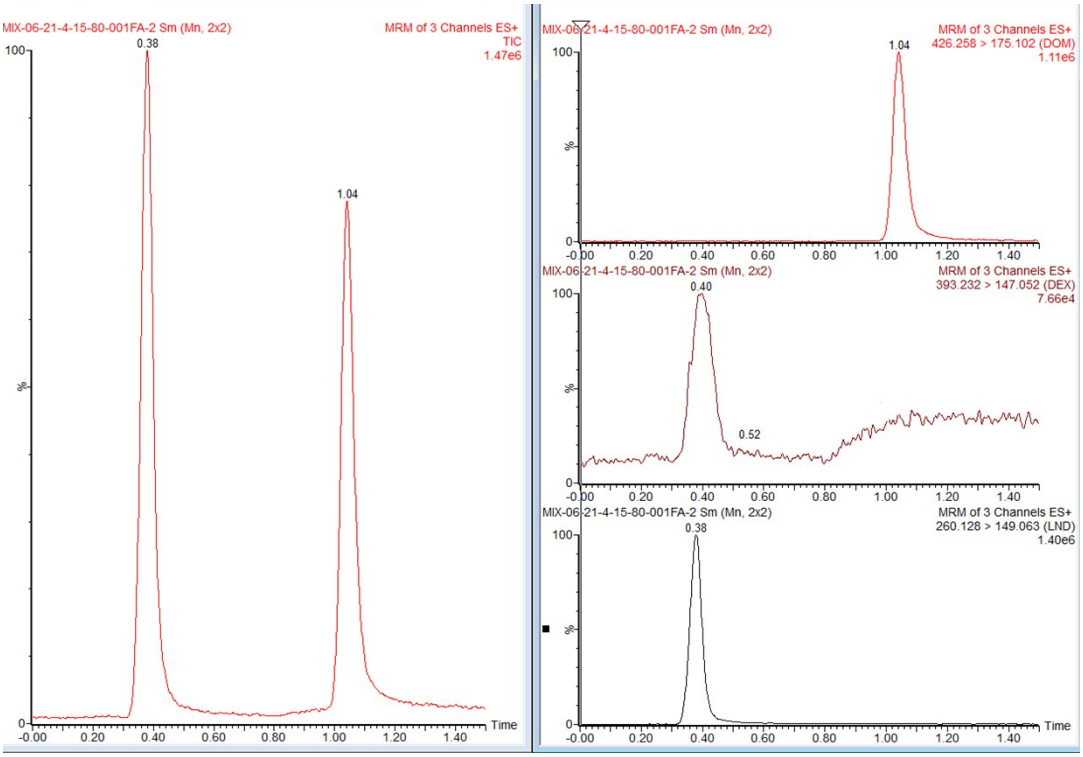
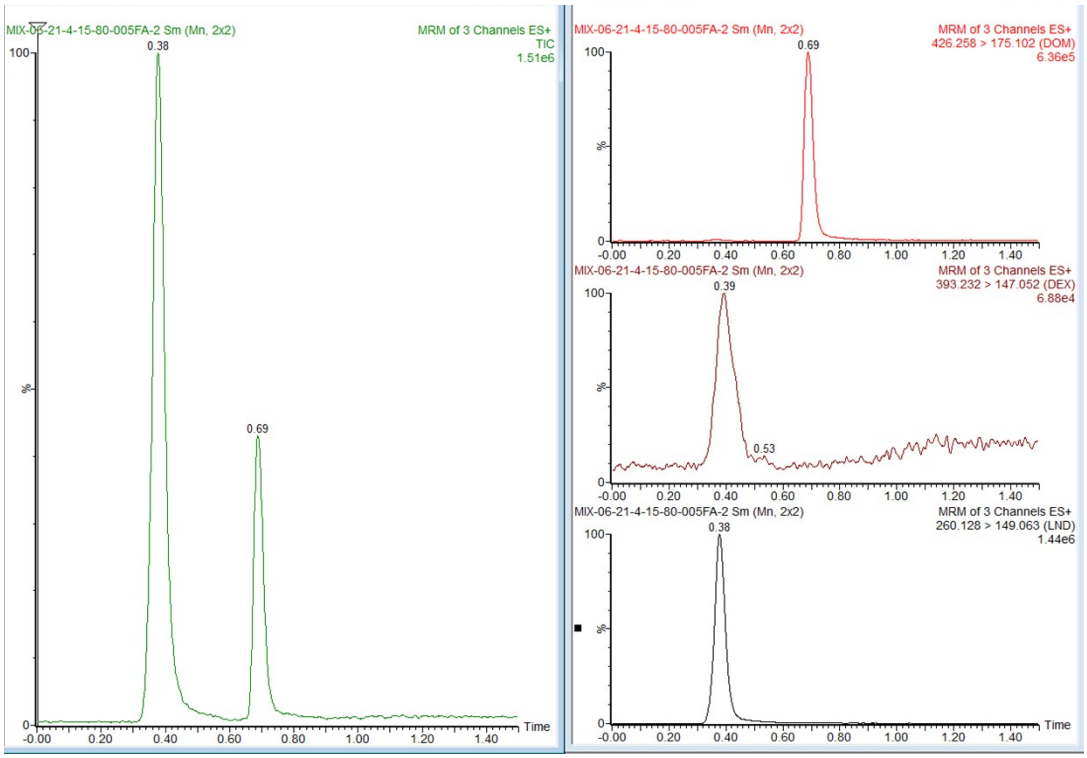


Fig. 1 TIC and MRM chromatograms of standard mixtures of DEX, LND, and OND (IS) showing the effect of acetonitrile% in the mobile phase, 30%, a), 40%, b), 50%, c), 60%, d), 70%, e), and 80%, f). All mobile phases were composed of mixtures of water and acetonitrile in different ratios, all with 0.1% formic acid.

a)


MIX-06-21-4-15-80-001FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
TIC
1.47e6
0.38
1.04
100
%
0
Time
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40
MIX-06-21-4-15-80-001FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
426.258 > 175.102 (DOM)
1.11e6
1.04
MIX-06-21-4-15-80-001FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
393.232 > 147.052 (DEX)
7.66e4
0.40
0.52
MIX-06-21-4-15-80-001FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
260.128 > 149.063 (LND)
1.40e6
0.38

b)


MIX-06-21-4-15-80-005FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
TIC
1.51e6
0.38
0.69
100
%
0
Time
-0.00 0.20 0.40 0.60 0.80 1.00 1.20 1.40
MIX-06-21-4-15-80-005FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
426.258 > 175.102 (DOM)
6.36e5
0.69
MIX-06-21-4-15-80-005FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
393.232 > 147.052 (DEX)
6.88e4
0.39
0.53
MIX-06-21-4-15-80-005FA-2 Sm (Mn, 2x2)
MRM of 3 Channels ES+
260.128 > 149.063 (LND)
1.44e6
0.38

c)

d)

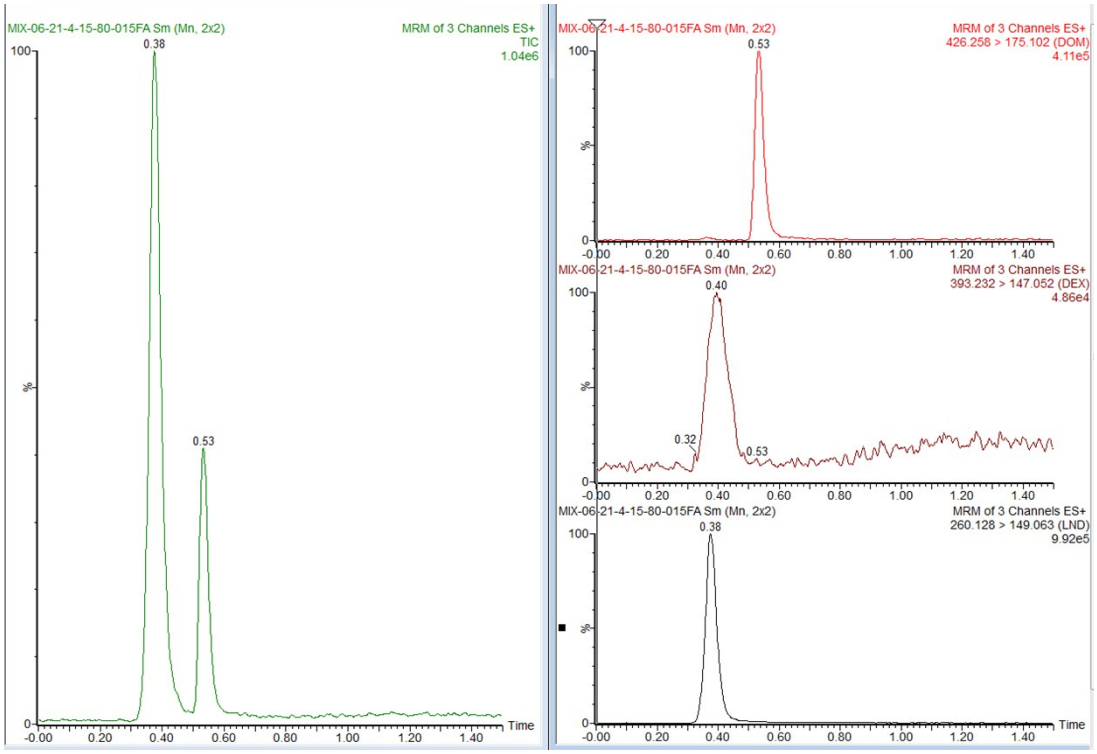


Fig. 2 TIC and MRM chromatograms of standard mixtures of DEX, LND, and OND (IS) showing the effect of formic acid% in the mobile phase, 0.01%, a), 0.05%, b), 0.1%, c), and 0.15%, d). All mobile phases were composed of mixtures of water and 80% acetonitrile with different percentage of formic acid.