

Simultaneous detection and quantification of angiotensin I, II, 1-7 and 1-9 by LC-MS/MS in human plasma

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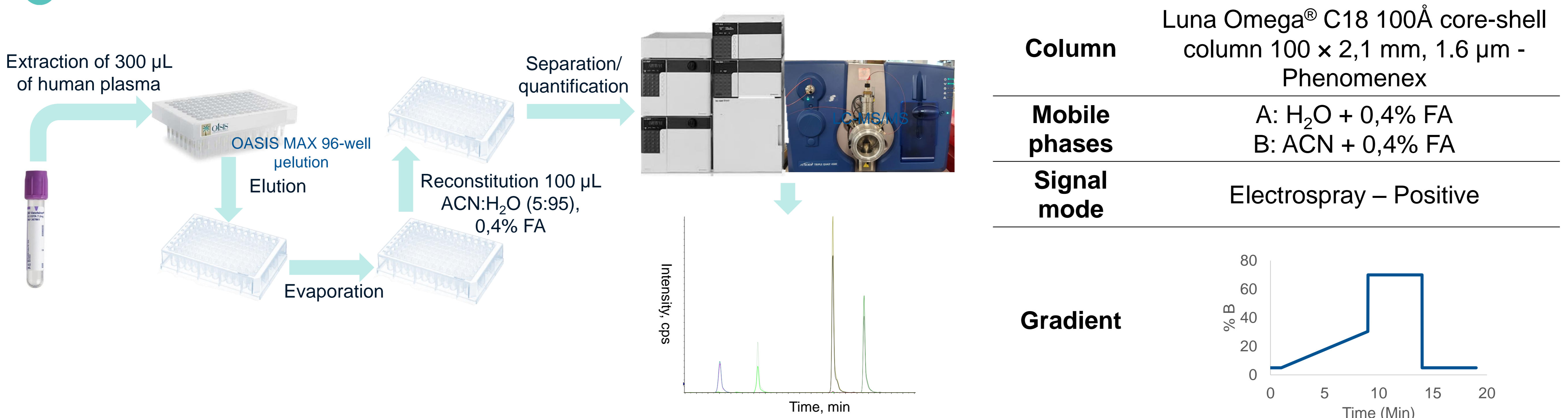
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Introduction:

Recent studies showed that angiotensin-converting enzyme 2 (ACE2) is used by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a cellular entry receptor. SARS-CoV-2 causes downregulation of ACE2 leading to renin-angiotensin-aldosterone system (RAAS) major imbalance. This is an essential element of unfavorable evolution in patients with COVID-19. With lower level of ACE2, cleavage of Ang I and Ang II is decrease and therefore, Ang 1-7 and Ang 1-9 levels are decreased. The development of a quantitative method for these angiotensins is particularly interesting in the context of the prognosis/follow-up of patients with COVID-19 [1-3].

Materials and Methods:

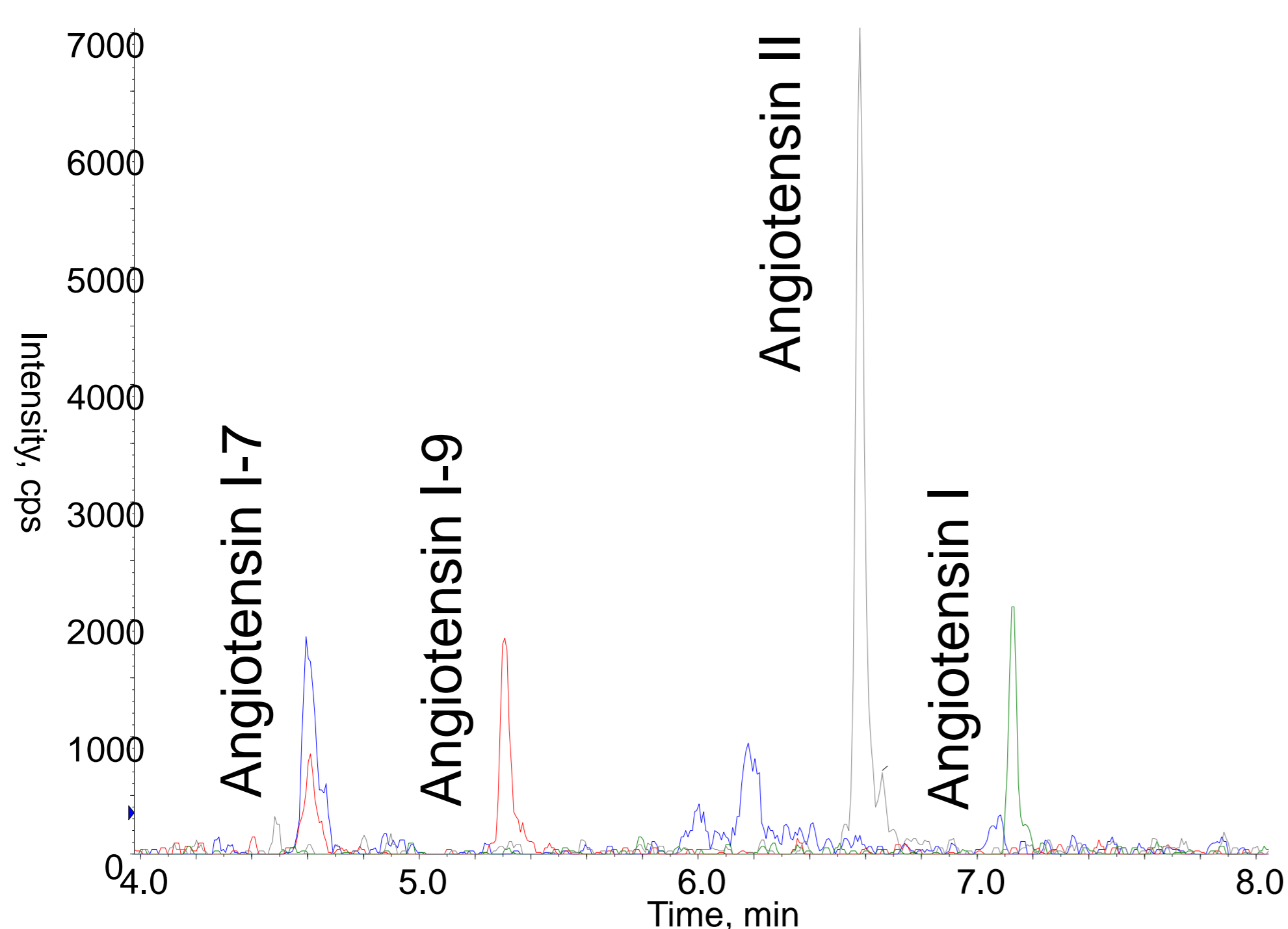


Results:

Q1 Scan – MRM – Post column flow injection

	Angiotensin I	Angiotensin II	Angiotensin 1-7	Angiotensin 1-9
Transitions	433,1 > 619,3	524,1 > 263,2	450,4 > 647,4	395,4 > 647,5
Compounds parameters	DP: 50,0 EP: 11,0 CXP: 22,0 CE: 27,0	DP: 50,0 EP: 11,0 CXP: 22,0 CE: 29,0	DP: 50,0 EP: 11,0 CXP: 22,0 CE: 24,0	DP: 50,0 EP: 11,0 CXP: 22,0 CE: 20,0
Source parameters	CUR: 40,0 CAD: Medium	IS: 2000,0 TEM: 650	GS1: 50,0 GS2: 60,0	

Lower Limit of quantification



Validation steps

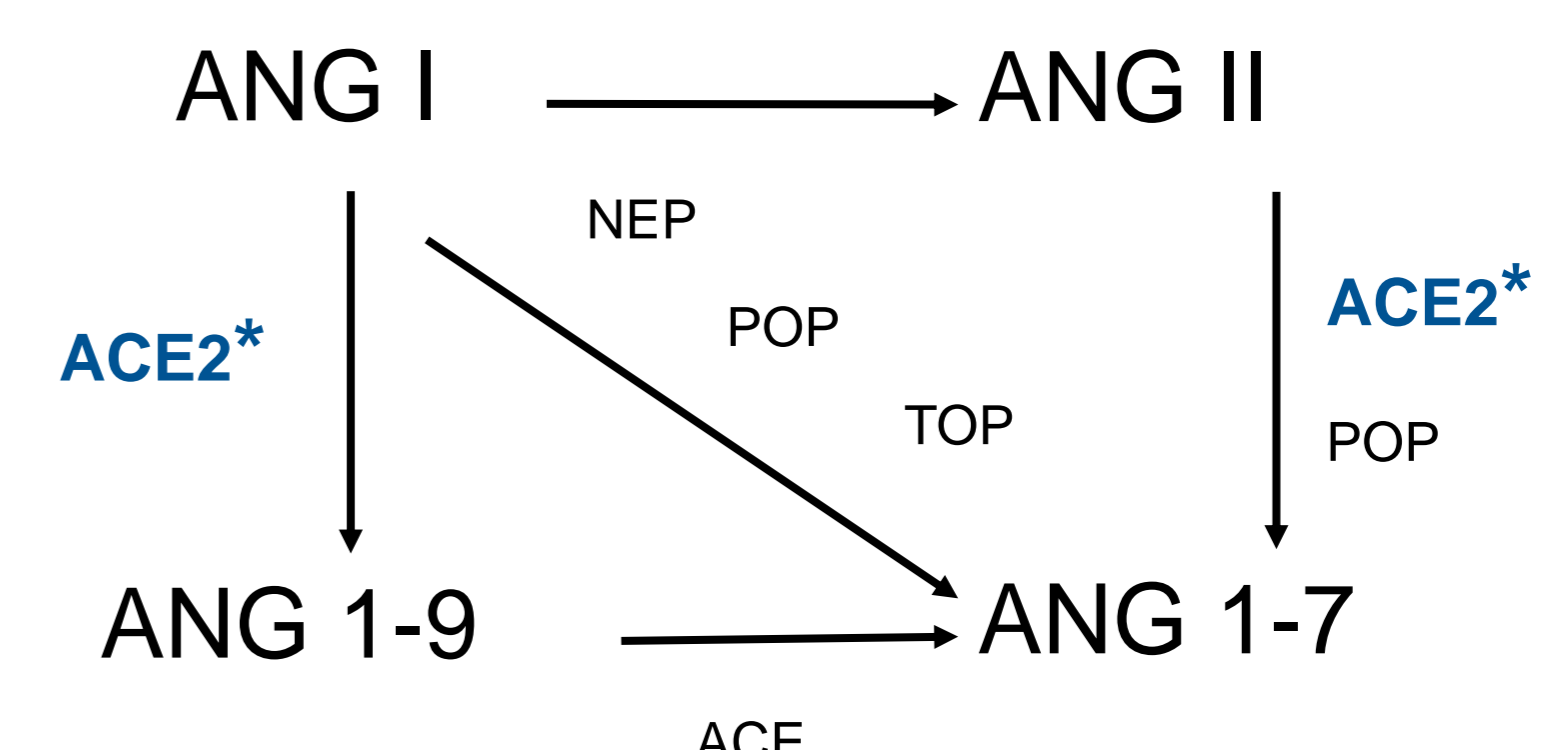
Recoveries	45-65%
Matrix effect	No matrix effect observed
Calibration curve	50 to 5,10 ⁴ pg/mL
LLOQ	50 pg/mL

Perspectives:

- Validation of the analytical method
- Addition of an incubation step to study the activity of ACE2

BUT ACE2* is a zinc finger enzyme

- ↳ EDTA precipitates zinc
- ↳ ACE2 is desactivated



References:

- Beyerstedt S, Barbosa Casaro E, Beuiloqua Rangel E – Covid 19; angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-COV-2 infection. European Journal of clinical Microbiology & infectious diseases 2021;40:905–919.
- Tikellis C, Bernardi S, Burns WC – Angiotensin-converting enzyme 2 is a key modulator of the renin-angiotensin system in cardiovascular and renal disease. Current opinion in nephrology and hypertension 2011; 20:62-68.
- Silhol F, Sarlon G, Deharo JC, Vaïsse B – Downregulation of ACE2 induces overstimulation of the renin-angiotensin system in COVID-19: should we block the renin-angiotensin system? Hypertension Research 2020; 43:854-856.