

Supporting Information

Table 1S Analytical methodologies reported in literature

S.No.	Matrix: Therapeutics	Degradant / Impurity	Mobile Phase	Column & its temp.	Mode of analysis & Detector wavelength	Diluent	Year (Ref.)
1.	Clinical Study	Metabolite	N/A	Atlantis dC18	HPLC-MS/MS	CH ₃ CN / MeOH,1:1	2011 (4)
2.	API	2 impurities	A: pH2, Sodium perchlorate buffer B: Acetonitrile-buffer (8:2), v/v	Purosphere, RP 18e 100mm×4.6mm,3.0 μm /45 °C	HPLC, 220nm	N/A	2016 (21)
3.	Tablets & API	MAC	Acetonitrile & 10 mM ammonium acetate (60:40, v/v)	Inertsil, 250×4.6mm, 5μm / 30°C	HPLC, 255 nm	Methanol (MeOH)	2014 (22)
4.	Tablets	MAC	Phosphate buffer, pH 3.6 & methanol (35:65, v/v)	C18, 250×4.6mm, 5μm / 25°C	HPLC, 268 nm	Mobile phase	2015 (23)
5.	Dissolution	MAC	0.16% Ammonium hydrogen carbonate(w/v), pH 9 and Acetonitrile (20:80, v/v)	Nucleodur C18, 250×3mm / 25 °C	HPLC, 260 nm	0.1%CTAB, pH 6.8	2009 (24)
	Pharmacokinetic study	Active metabolite & MAC	A: 0.1% Formic acid B: 0.1% Acetonitrile (CH ₃ CN)	XTerra MS C18, 50mm ×2.1mm, 3.5μm	HPLC-MS/MS	CH ₃ CN / MeOH	
6.	Clinical Study	Active metabolite & MAC	Acetonitrile and 0.2% formic acid (65: 35, v/v)	Inertsil ODS-SP, 100 mm×2.1 mm, 3.5μm/30°C	LC-MS/MS	CH ₃ CN	2015 (25)
7.	Clinical Study	Active metabolite, MAC & Bosentan	0.1% Formic acid and acetonitrile	Luna C8, 20 mm×2.0 mm, 5μm/25°C	HPLC-MS/MS	Ethanol / CH ₃ CN,1:1	2014 (26)
8.	Pharmacokinetic study	MAC	0.2% formic acid and methanol	UPLC BEH C18 column (2.1 mm × 100 mm, 1.7 μm)	UPLC-MS/MS	CH ₃ CN	2015 (27)
9.	Clinical Study	2 active metabolites & MAC	N/A	N/A	HPLC-MS/MS	MeOH / DMSO	2012 (28)

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10	API	MAC & 4 impurities	A: acetonitrile-water-formic acid (50-50-0.1) B: acetonitrile-water-formic acid (85-15-0.1)	Agilent C18 column (250 mm × 4.6 mm, 5µm)	RP-HPLC	Mobile phase A	2017 (29)
11	API	MAC	A:0.02% trifluoroacetic acid B:acetonitrile	Inertsil C18 column (150 × 4.6 mm, 5 µm)	RP-HPLC	H ₂ O: CH ₃ CN,1:1	2018 (30)

N/A: Not Applicable (no information available); Ref.: Reference

The above table describes the information of available literature methods which are related to Macitentan drug (MAC), (to the best of our knowledge).