Structural elucidation and synthesis of a dimeric degradation impurity during long-term stability studies of oxycodone hydrochloride injection

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Supplementary material

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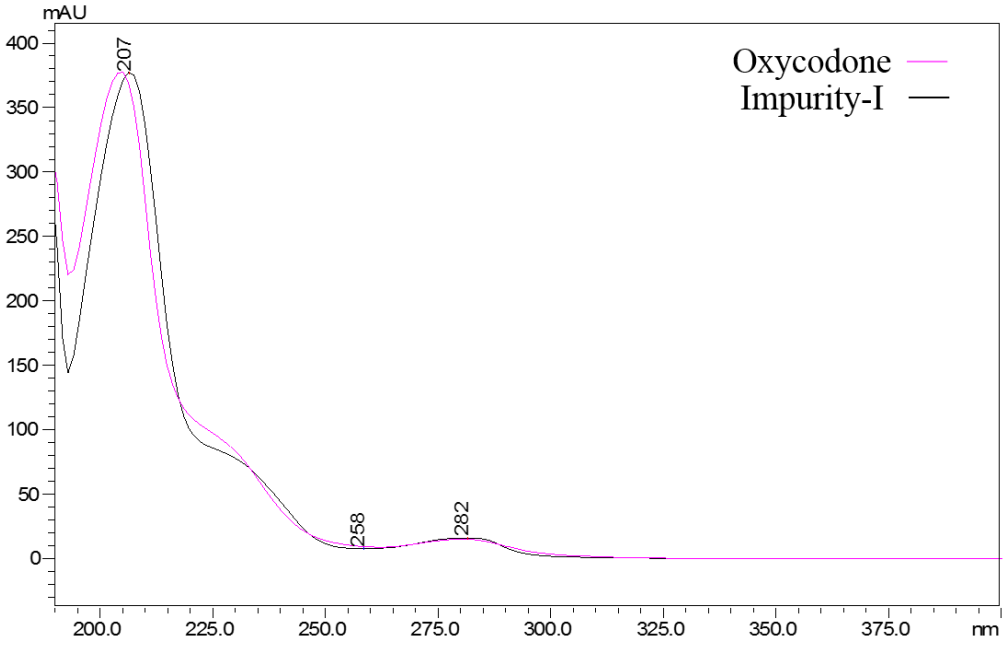

Fig. S1. UV spectra of oxycodone and impurity-I.

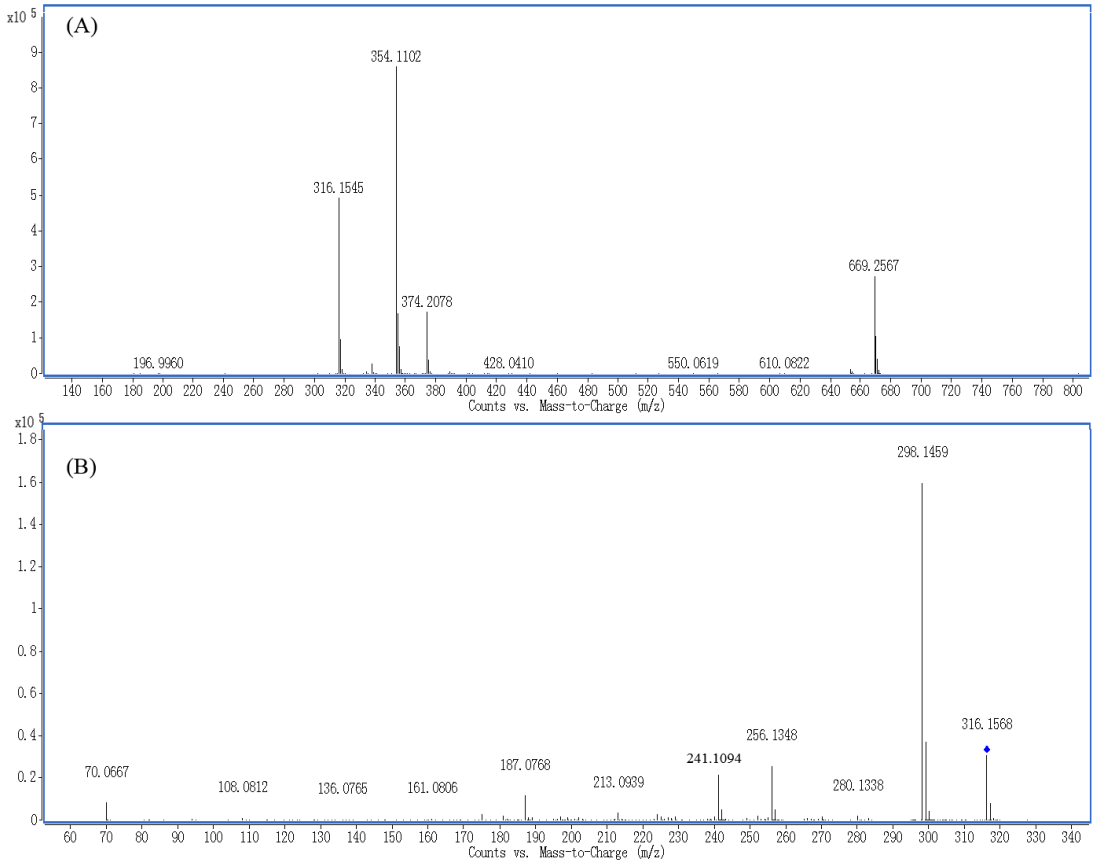

Fig S2. The (+)-HR-ESI-MS, MSMS spectra of oxycodone

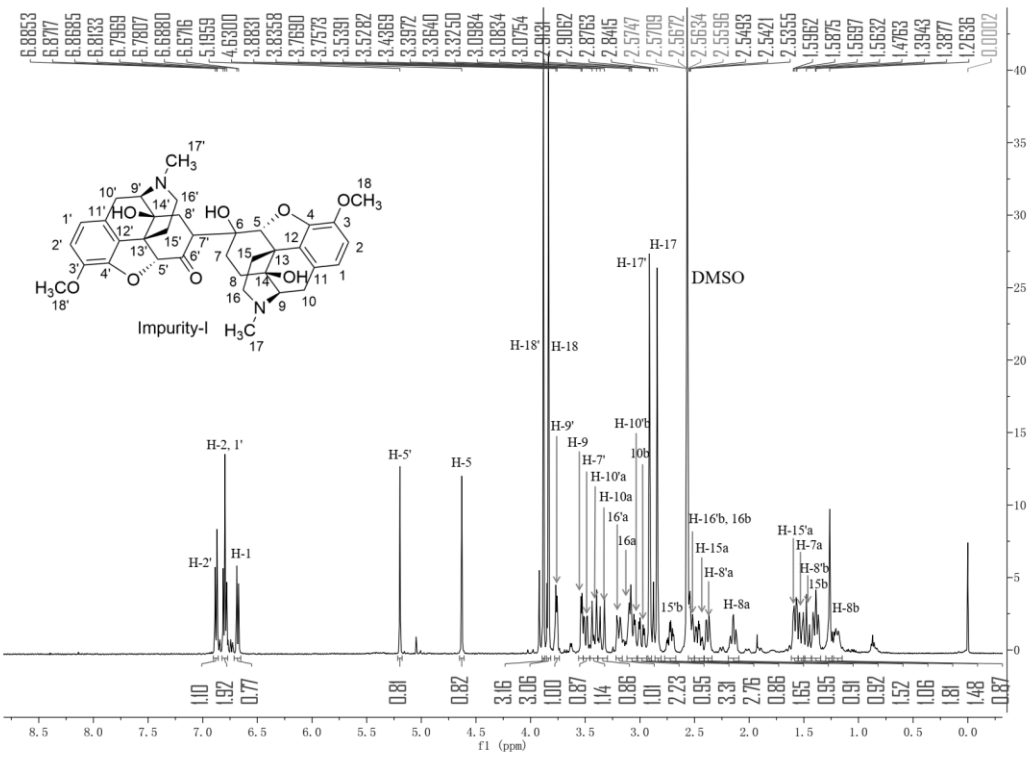

Fig S3. ^{1}H NMR spectrum of impurity-I (500 MHz, DMSO-d_6 + TFA-d)

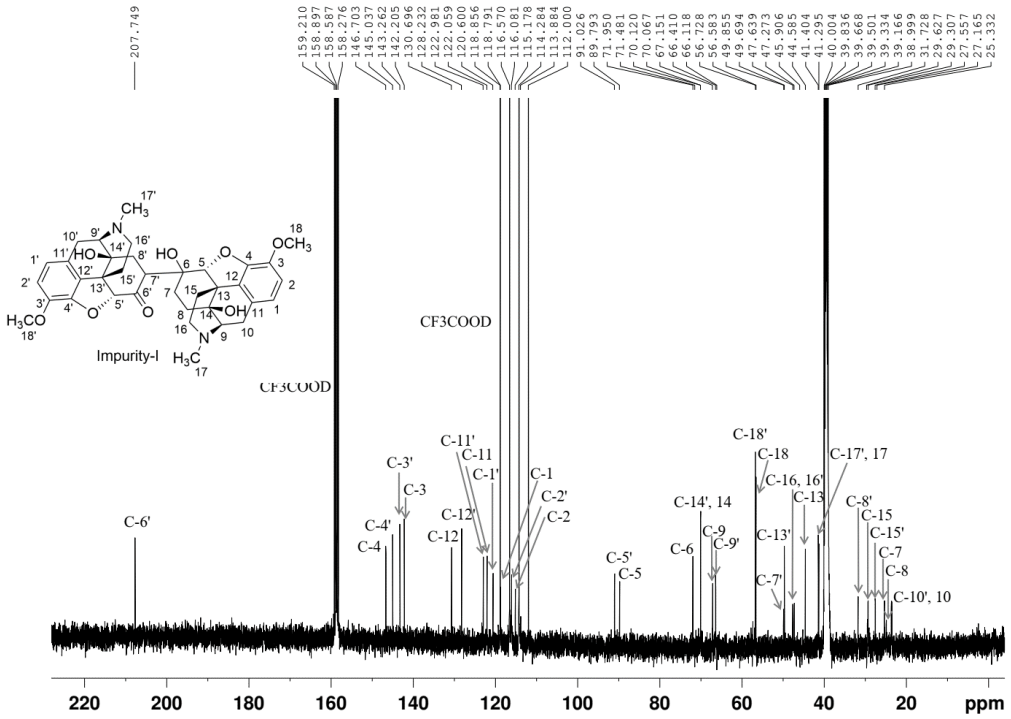

Fig S4. ^{13}C NMR spectrum of impurity-I (125 MHz, DMSO-d_6 + TFA-d)

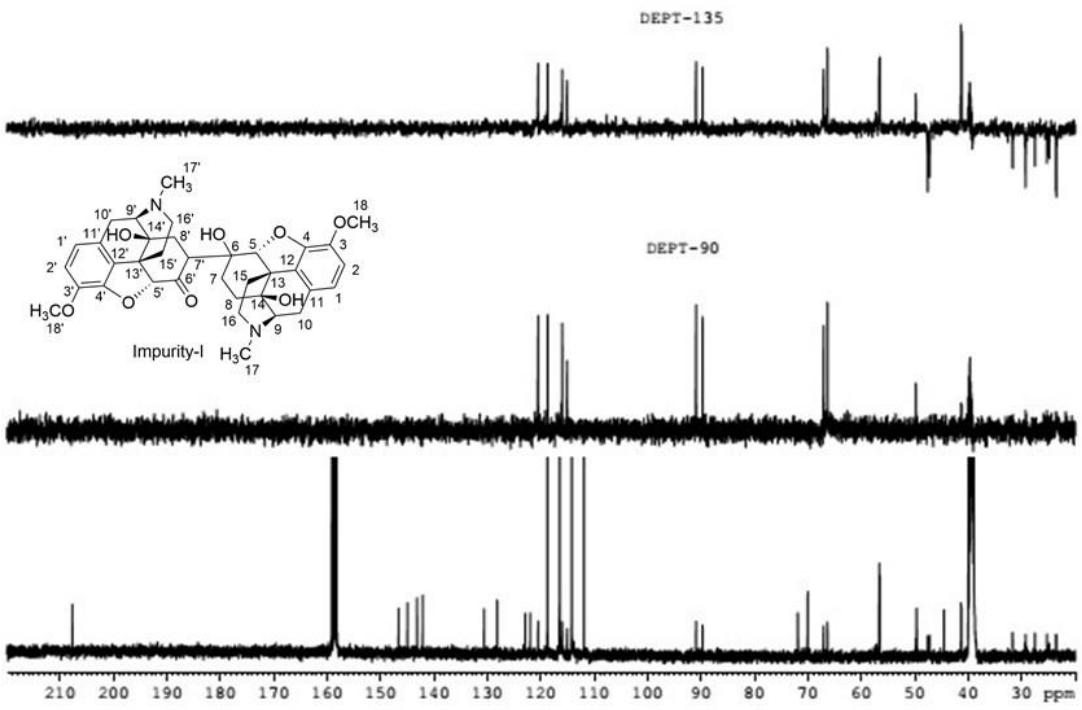

Fig S5. DEPT 90 and DEPT 135 spectra of impurity-I (125 MHz, DMSO-d_6 + TFA-*d*)

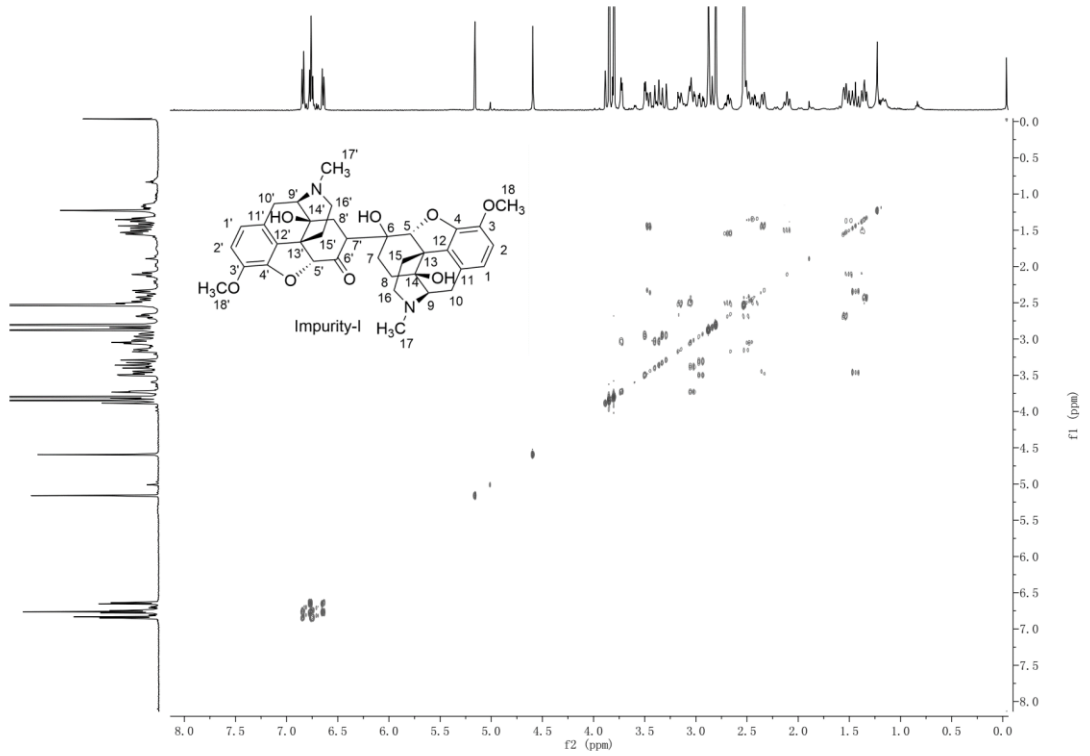

Fig S6. ^{1}H-^{1}H COSY spectrum of impurity-I (500 MHz, DMSO-d_6 + TFA-*d*)

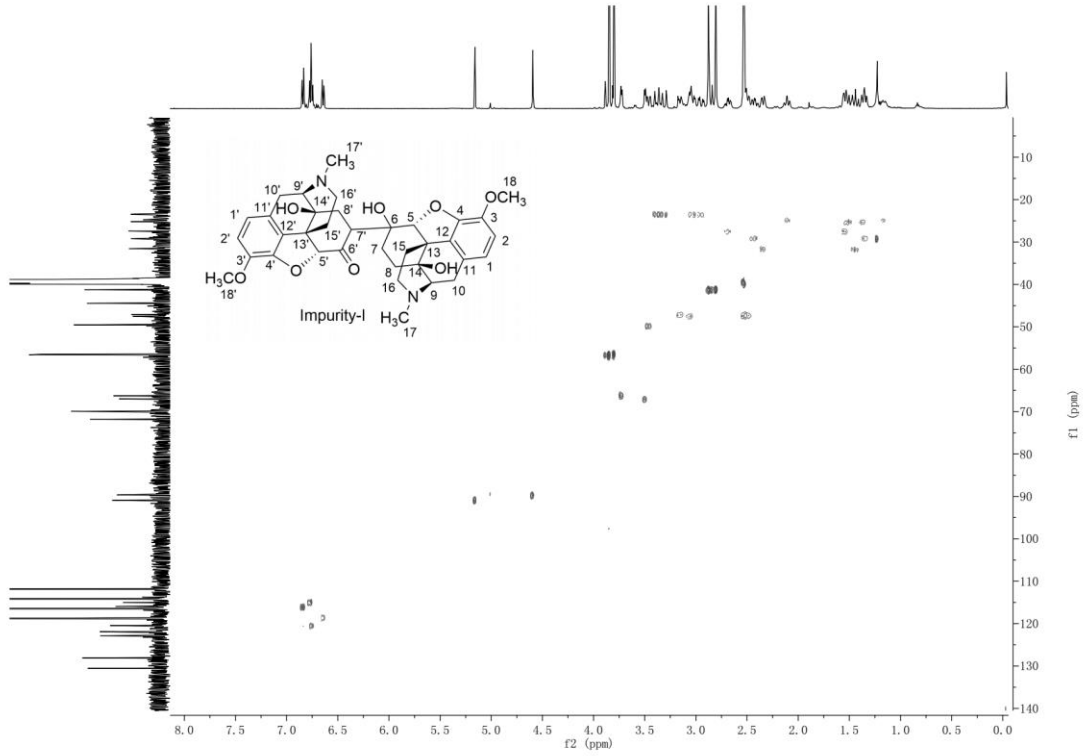

Fig S7. HSQC spectrum of impurity-I (500 MHz, DMSO-d_6 + TFA-d)

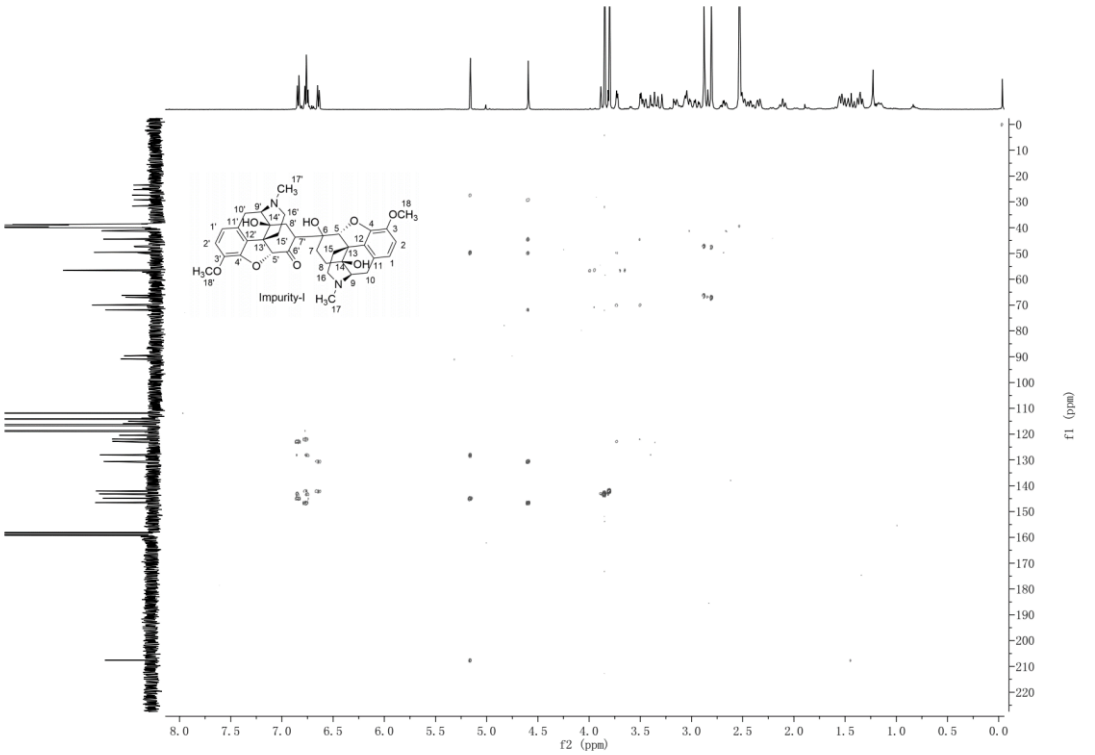

Fig S8. HMBC spectrum of impurity-I (500 MHz, DMSO-d_6 + TFA-d)

Table S1. Probability values of different toxicity models of oxycodone and impurity-I by TOPKAT analyses

Model	**Oxycodone**	**Impurity-I**
NTP carcinogenicity call (male rat) (v3.2)	0.992	1.000
NTP carcinogenicity call (female rat) (v3.2)	0.000	0.000
NTP Carcinogenicity Call (Male Mouse) (v3.2)	0.000	1.000
NTP Carcinogenicity Call (Female Mouse) (v3.2)	0.000	0.000
FDA Carcinogenicity Male Rat Non vs Carc (v3.1)	0.000	0.000
FDA Carcinogenicity Male Rat Single vs Mult (v3.1)	0.000	0.000
FDA Carcinogenicity Female Rat Non vs Carc (v3.1)	0.000	0.000
FDA Carcinogenicity Female Rat Single vs Mult (v3.1)	0.000	0.000
FDA Carcinogenicity Male Mouse Non vs Carc (v3.1)	0.000	0.053
FDA Carcinogenicity Male Mouse Single vs Mult (v3.1)	0.000	0.000
FDA Carcinogenicity Female Mouse Non vs Carc (v3.1)	0.000	1.000
FDA Carcinogenicity Female Mouse Single vs Mult (v3.1)	0.000	0.000
Weight of Evidence Carcinogenicity Call (v5.1)	0.189	0.000
Ames Mutagenicity (v3.1)	0.000	0.004
Developmental Toxicity Potential (v3.1)	0.001	0.726
Rat Oral LD_{50} (v3.1)	812.0 mg/kg	16.5 μg/kg
Rat Maximum Tolerated Dose – Feed/Water (v6.1)	263.1 mg/kg	0.1 pg/kg
Rat Maximum Tolerated Dose – Gavage (v6.1)	263.1 mg/kg	0.3 pg/kg
Rat Inhalational LC_{50} (v6.1)	3.4 $g/m^3/H$	183.9 $mg/m^3/H$
Chronic LOAEL (v3.1)	470.1 mg/kg	1.5 μg/kg
Skin Irritation (v6.1)	0.795	0.000
Skin Sensitization NEG v SENS (v6.1)	0.000	1.000
Skin Sensitization MLD/MOD v SEV (v6.1)	0.000	0.000
Ocular Irritancy SEV/MOD vs MLD/NON (v5.1)	1.000	0.000
Ocular Irritancy SEV vs MOD (v5.1)	0.000	1.000
Ocular Irritancy MLD vs NON (v5.1)	1.000	0.992
Aerobic Biodegradability (v6.1)	0.001	1.000
Fathead Minnow LC_{50} (v3.2)	456.1 μg/l	80.0 ng/l
Daphnia EC_{50} (v3.1)	511.4 g/l	1000 g/l