## Study on the stabilization mechanisms of wet-milled cepharanthine nanosuspensions using systematical characterization

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## **Supplementary Figure:**

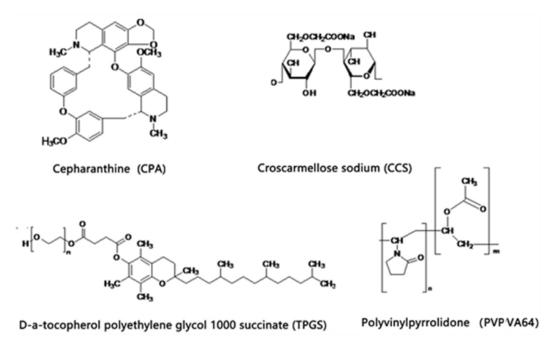


Figure S1 Chemical structures of Cepharanthine (A), CCS (B), TPGS (C) and PVP VA64 (D).

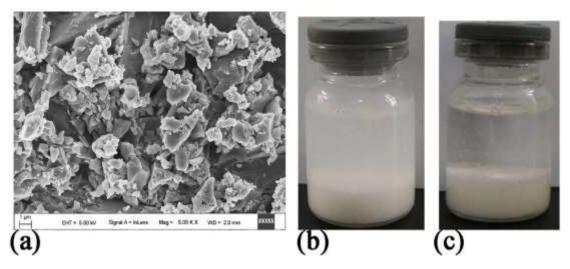


Figure S2. SEM image of raw CPA(a), representative images of milled suspension without stabilizer during storage within 1 min (b) and 15 min (c) at  $4 \square$ .

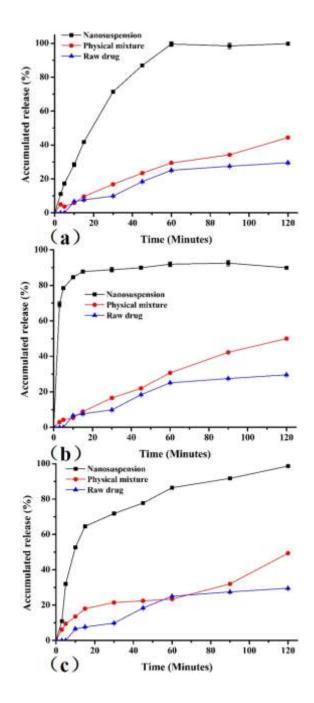
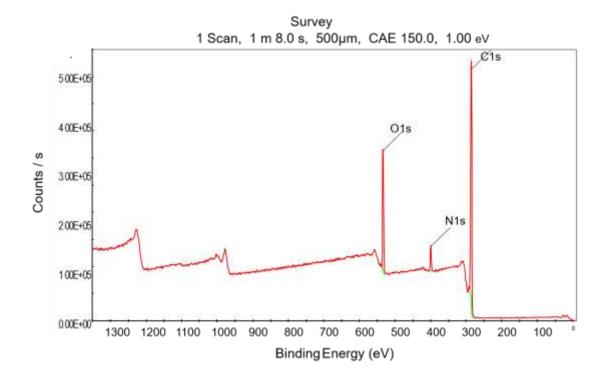
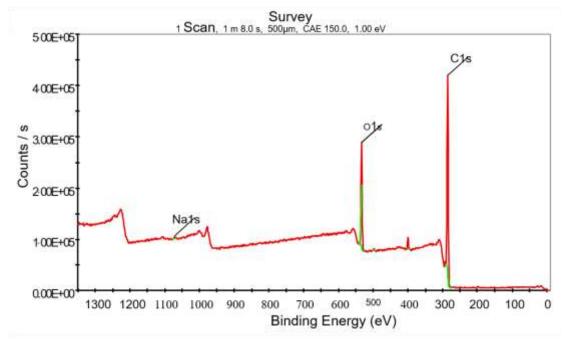


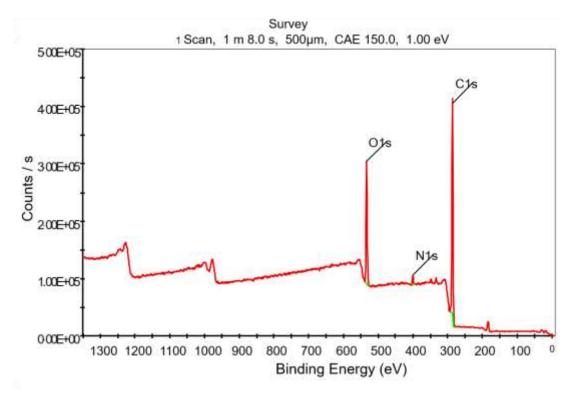
Figure S3 Dissolution profiles of different formulations. (a) Dissolution profiles of raw
drug, CCS-CPA physical mixture and corresponding nanosuspension. (b) Dissolution
profiles of raw drug, TPGS-CPA physical mixture and corresponding nanosuspension.
(c) Dissolution profiles of raw drug, PVP VA64-CPA physical mixture and
corresponding nanosuspension.



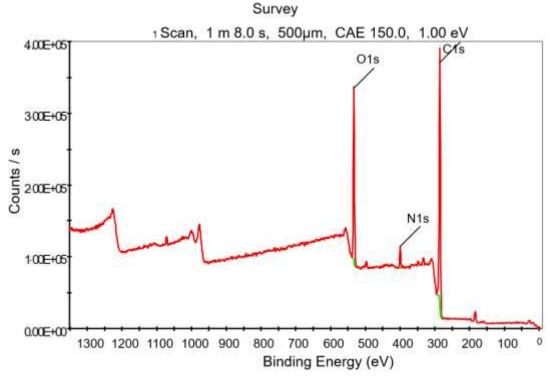
(a)







(c)



(d)

Figure S4 Survey scan (0-1300 eV) scanning of pure CPA (a), CCS-CPA NS (b), TPGS-

CPA NS (c) and PVP VA64-CPA NS (d).

## Supplementary Tables

Formulation	Stabilizer	Rotating speed (rpm)	Time (min)	Drug: Stabilizer (w/w)
CCS-CPA NS	CCS	2400	30	5:1
TPGS-CPA NS	TPGS	2400	30	5:1
PVP VA64-CPA NS	PVP VA64	2400	30	5:1

Table S1. Formulations and process parameters of the milled drug suspensions.

Table S2. Similarity factor values of each two of release profiles from pure CPA,

Formulation	$f_2$		
	CCS	TPGS	PVP VA64
physical mixture <sup>a</sup>	57.32	59.28	58.14
Nanosuspensions <sup>b</sup>	14.92	9.65	36.21

physical mixture and nanosuspension.

a: compared with pure CPA

b: compared with the corresponding physical mixture