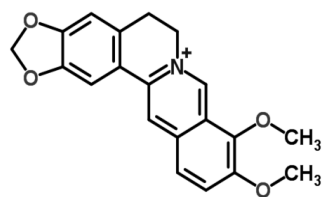
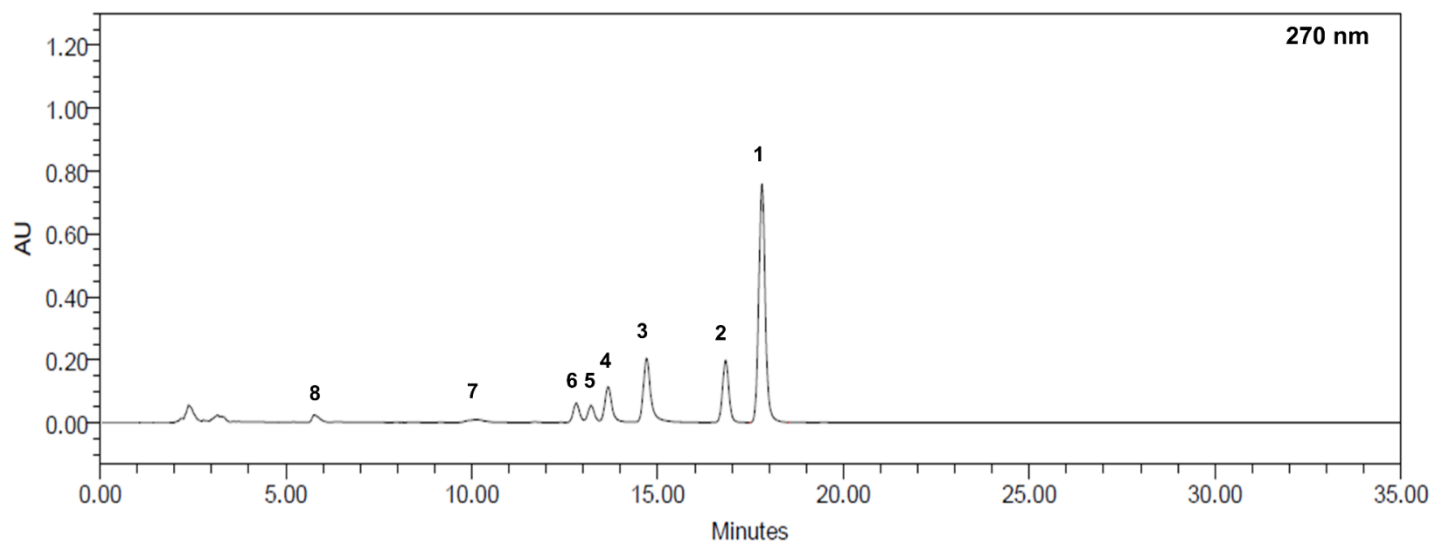
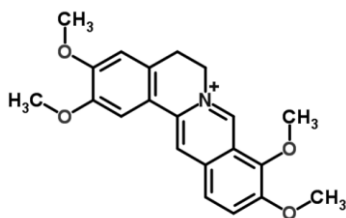


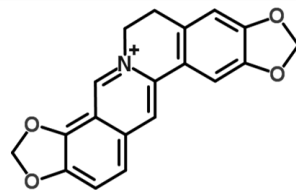
Supplementary File 1. Chemical analysis and HPLC fingerprint of RCEG.



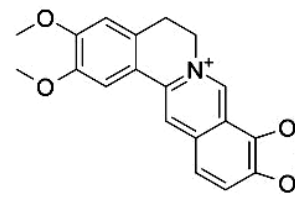
1. Berberine



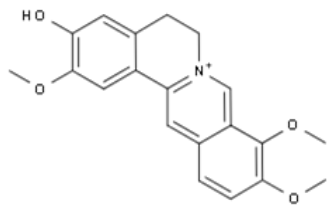
2. Palmatine



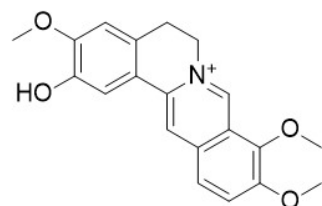
3. Coptisine



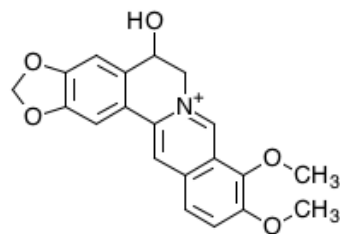
4. Epiberberine



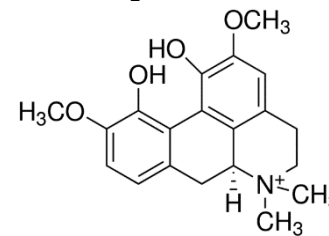
5. Jatrorrhizine



6. Columbamine



7. Berberastine



8. Magnoflorine

RCEG was produced by Sun Ten Pharmaceutical Co., LTD., a GMP manufacturer of herbal extract conforming to international standards. The chemical composition of *Rhizoma Coptidis* was analyzed using HPLC with photodiode array (PDA) detection. The sample preparation included mixing 0.1 g of *Rhizoma Coptidis* with 40 ml of methanol/water solution (70%/30%, v/v), ultra-sonicating at 25°C for 15 mins and then shaking at 160 rpm in a 40°C water bath for 20 mins. After centrifugation and filtration, 20 µl of sample solution was analyzed via HPLC. A Cosmosil 5C18-MS-II column was utilized as the stationary phase, and a gradient of mixture of sodium dodecyl sulfate (SDS), sodium acetate, acetic acid, acetonitrile, and water were used as the elute solution. The UV detection wavelength was set at 270 nm. The analytical run time was 35 mins. Eight peaks representing berberine, palmatine, coptisine, epiberberine, jatrorrhizine, columbamine, berberastine and magnoflorine were numbered in the chromatograms and their chemical structures were displayed accordingly. Berberine is the indicative compound of *Rhizoma Coptidis*. The following table summarizes the batch numbers of RCEG used in Chinese medicine clinics in the Taipei, Linkou, and Taoyuan branches of Chang Gung Memorial Hospital from January 1, 2008 to November 30, 2017. The berberine of RCEG in different batches from the same manufacturer were quantified among 45 to 50 mg/g. HPLC, high performance liquid chromatography; RCEG, *Rhizoma Coptidis* extract granules.

Years	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Batch number of <i>Rhizoma Coptidis</i> extract granules	052914	023411	055306	040108	050805	13020107	13083007	14081508	15091003	16103109
	163107	163107	114508	060508	050806	13020108	14011703	14121811	16012009	16110110
	252410	183410	114912	060509	080810	13052909	14011704	14121907	16012204	16110209
	272409	184406	134906	070105	131602	13052911	14011706	15041411	16012506	17032106
	312011	203708	235206	230309	131610	13053006	14041003	15041508	16012507	17032107
		314410		235611	141606	13083007	14041009	15041603	16061303	17032209
				245612	231207	271905	14041106	15042007	16062709	17062108
				275607	271905	301909	14041107	15090310	16062710	17062109
						301910	14081409	15090909	16062807	17062206
							14081410	15091003		
						14081507				