Supplementary File 1. Inclusion and exclusion criteria.

The subjects had no potential difficult airway problems nor had previously experienced serious primary diseases of vital organs, including liver, kidney, digestive tract, hemopathy or metabolic disorders.

The exclusion criteria included allergy to either propofol or the ciprofol emulsion components (soybean oil, glycerin, triglycerides, egg yolk lecithin, sodium oleic acid and sodium hydroxide). Subjects who had a history of substance abuse, any symptoms of long-term use of benzodiazepines drugs, or a positive urine drug test were also excluded. Pregnant and lactating females or those who did not want to use medically acceptable forms of birth control during the entire course of the study were also excluded.

Supplementary File 2. AE and SAE definitions.

The Investigator used clinical judgment to determine the relationship between AEs and the investigational drug. Alternative causes, such as natural history of the underlying diseases, concomitant therapy, other risk factors, and the temporal relationship of the event to the investigational product was considered and investigated. The causal relationship of an AE to the investigated drug was assessed by the investigator (or medically qualified delegate) using the classifications provided in the Supplementary Table 1.

A SAE was any untoward medical occurrence at any dose: 1) resulted in death; 2) was life threatening (i.e. the subject was at immediate risk of death at the time the event occurred; it did not refer to an event which might hypothetically have caused death had it been more severe); 3) required in-subject hospitalization or prolongation of existing hospitalization; 4) resulted in persistent or significant disability/incapacity; 5) was a congenital anomaly/birth defect; 6) was a medically important event or reaction.

Supplementary Table 1. Classification of AEs as associated with drug

Indicator	Definitely related	Probably related	Possible related	Possible not related	Not related
Reasonable time sequence	Yes	Yes	Yes	Yes	Yes
Belongs to the type of reaction known to the study drug	Yes	Yes	Yes	No	No
Reaction may be improved after discontinuation of the study drug	Yes	Yes	Yes or No	Yes or No	Yes or No
Reaction may re-occur with medication	Yes	?	?	?	No
There is another explanation for the reaction	No	No	Yes	Yes	Yes

Supplementary File 3. Plasma sampling and PK measurements.

At first, 100 μL plasma samples were pretreated for protein precipitation. Then, the plasma concentration of ciprofol was determined using a method of validated liquid chromatography (HPLC; Agilent 1260, Agilent Technologies, Wilmington, DE)-tandem mass spectrometry (LC-MS/MS; API 5500 mass spectrometer, SCIEX, Foster City, CA). The retention time of ciprofol was about 1.6 min, and the calibration curve was calculated by linear regression of the ciprofol peak area (weighting factor $1/x^2$), with a linear range of 5.00 ng/mL to 5,000 ng/mL. All plasma concentration data were acquired and processed by Analyst 1.5.2 (Applied Biosystem, CA, US) and Watson LIMS V7.2.0.02 (PSS, Inc, Wayne, PA) software. The plasma pharmacokinetic parameters, including C_{max}, $AUC_{0\text{-}30\ min}$, $AUC_{0\text{-}1\ h}$, $AUC_{0\text{-}inf}$, T_{max}, Vz $T_{1/2Z}$, clearance (CL) and mean residence time (MRT) were calculated by a non-compartment model 10. Systemic exposure was estimated as the area under the curve ($AUC_{0\text{-}t}$) from the time of dosing to the last measurable time point (t) by application of the trapezoidal rule using the following equation: $AUC_{(i,\ i+1)} = (T_{i+1}\text{-}T_i)(C_i+C_{i+1})/2$ where $AUC_{0\text{-}t}$ is the sum of all $AUC_{(i,\ i+1)}$. The area under the first moment curve was estimated similarly and extrapolated to infinity according to the following equation: $AUC_{0\text{-}\infty} = AUC_{0\text{-}t} + C_t/\lambda_z$. Of which, C_t was the final determination of plasma concentration. And λz was an elimination rate constant, which is the slope of the end segment for the semi-log plasma concentration-time curve calculated using the linear regression method.

Supplementary Table 2. Modified quality of recovery-9 (QoR-9) questionnaire

QoR-questions	Not at all	Some of time	Most of time
Had a feeling of general well-being	0	1	2
Had support from others (especially doctors and nurses)	0	1	2
Been able to understand instructions and advice. Not being confused	0	1	2
Had a feeling can look after personal toilet and hygiene unaided	0	1	2
Had a feeling can pass urine and having no trouble with bowel function	0	1	2
Been able to breathe easily	0	1	2
Been free from headache, backache or muscle pains	0	1	2
Been free from nausea, dry-retching or vomiting	0	1	2
Been free from experiencing severe pain, or constant moderate pain	0	1	2
Summary score			18

Supplementary File 4. Data acquisition and management.

The Electronic Data Capture (EDC) System was employed in this trial and an electronic case report form (eCRF) was used to collect the data specified in the protocol: the Clinical Study Coordinator (CRC), designated by the principal investigator (PI), timely and accurately input the data from the original medical records into the eCRF, then the data were simultaneously logically-checked by the EDC, and textual data were also manually checked by the data administrator. Once the data from all subjects had been completely and accurately entered, they were reviewed by the PI, sponsor, statisticians and data administrator again to confirm the integrity and accuracy of the database, and finally the database was locked by the data administrator. Subsequently, the data administrator imported appropriate data into the specified database and submitted it to statisticians for statistical analyses.

Supplementary Table 3. Laboratory examinations

	0.40 mg/kg (n = 6)	0.60 mg/kg (n = 6)	0.90 mg/kg (n = 6)
Blood routine			
Hemoglobin (g/L)			
Baseline	147.0 (124.0, 151.0)	142.5 (138.0, 157.0)	145.5 (136.0, 156.0)
24 h of after administration	145.5 (118.0, 151.0)	136.5 (132.0, 155.0)	145.0 (132.0, 158.0)
Red blood cell (10^{12}/L)			
Baseline	4.92 (4.25, 5.11)	4.85 (4.60, 5.05)	4.95 (4.59, 5.20)
24 h of after administration	4.87 (3.99, 5.02)	4.70 (4.57, 4.99)	4.85 (4.56, 5.19)
Platelet count (10^9/L)			
Baseline	258.5 (249.0, 294.0)	205.5 (170.0, 233.0)	224.5 (204.0, 250.0)
24 h of after administration	235.0 (208.0, 269.0)	208.5 (168.0, 261.0)	207.0 (196.0, 221.0)
White blood cell (10^9/L)			
Baseline	5.64 (4.62, 6.94)	5.22 (4.67, 6.23)	5.42 (4.37, 6.26)
24 h of after administration	4.86 (4.31, 7.39)	5.39 (4.95, 6.35)	4.76 (4.46, 6.82)
Neutrophils (%)			
Baseline	58.5 (56.9, 61.7)	57.3 (55.1, 61.0)	57.0 (52.5, 58.9)
24 h of after administration	60.6 (56.2, 65.9)	57.3 (55.3, 60.0)	58.0 (53.4, 64.4)
Lymphocytes (%)			
Baseline	33.0 (32.0, 33.3)	33.9 (27.6, 35.8)	35.0 (31.1, 36.8)
24 h of after administration	30.9 (26.5, 34.4)	33.2 (30.7, 35.8)	32.8 (25.6, 35.9)
Monocytes (%)			
Baseline	5.80 (5.40, 6.00)	7.05 (6.10, 7.40)	6.45 (5.50, 8.10)
24 h of after administration	5.80 (5.20, 5.90)	6.30 (5.40, 6.80)	6.75 (5.70, 8.30)

Hematocrit (L/L)			
Baseline	0.43 (0.39, 0.44)	0.43 (0.40, 0.45)	0.45 (0.40, 0.46)
24 h of after administration	0.43 (0.36, 0.44)	0.41 (0.39, 0.45)	0.44 (0.41, 0.47)
Blood biochemistry			
Aspartate transaminase (IU/L)			
Baseline	19.0 (18.0, 25.0)	19.5 (19.0, 22.0)	20.0 (19.0, 26.0)
24 h of after administration	18.0 (16.0, 19.0)	17.5 (17.0, 19.0)	19.0 (18.0, 23.0)
Alanine transaminase (IU/L)			
Baseline	17.5 (11.0, 21.0)	12.0 (11.0, 19.0)	16.5 (13.0, 24.0)
24 h of after administration	16.0 (9.0, 22.0)	11.5 (8.0, 16.0)	14.5 (10.0, 23.0)
Alkaline phosphatase (IU/L)			
Baseline	59.0 (52.0, 69.0)	58.5 (53.0, 74.0)	62.0 (60.0, 70.0)
24 h of after administration	56.5 (52.0, 64.0)	54.5 (49.0, 61.0)	55.0 (54.0, 73.0)
Lactate dehydrogenase (IU/L)			
Baseline	182.5 (159.0, 196.0)	157.0 (147.0, 160.0)	173.0 (164.0, 192.0)
24 h of after administration	163.5 (137.0, 174.0)	148.0 (131.0, 168.0)	167.5 (160.0, 171.0)
Total protein (g/L)			
Baseline	74.5 (72.6, 75.8)	76.1 (72.9, 79.0)	77.7 (74.1, 79.2)
24 h of after administration	72.6 (67.3, 74.1)	71.5 (70.3, 74.4)	75.5 (73.4, 77.8)
Albumin (g/L)			
Baseline	48.3 (46.7, 49.5)	50.6 (48.9, 52.9)	49.0 (47.5, 49.6)
24 h of after administration	45.7 (44.4, 46.8)	47.5 (45.0, 49.9)	47.2 (45.3, 48.6)
Total bilirubin (μmol/L)			
Baseline	12.3 (11.3, 16.5)	14.9 (12.5, 18.0)	10.8 (9.9, 12.7)
24 h of after administration	10.6 (9.8, 13.6)	14.0 (10.2, 20.5)	13.4 (9.8, 14.5)
Ureophil (mmol/L)			
Baseline	3.81 (3.50, 5.50)	5.00 (3.80, 6.19)	4.10 (3.36, 4.60)
24 h of after administration	4.00 (3.60, 4.40)	3.85 (3.50, 4.30)	3.68 (3.30, 5.10)
Creatinine (μmol/L)			
Baseline	76.0 (52.0, 90.0)	64.5 (53.0, 73.0)	63.5 (56.0, 66.0)
24 h of after administration	59.5 (37.0, 77.0)	65.0 (49.0, 81.0)	70.0 (54.0, 72.0)
Uric acid (μmol/L)			
Baseline	424.0 (276.0, 476.0)	366.0 (230.0, 403.0)	310.0 (268.0, 387.0)
24 h of after administration	393.0 (235.0, 482.0)	321.5 (247.0, 349.0)	303.5 (253.0, 329.0)
K (mmol/L)			
Baseline	4.14 (3.97, 4.28)	4.08 (4.00, 4.28)	4.07 (3.89, 4.23)
24 h of after administration	4.08 (3.97, 4.22)	4.31 (4.07, 4.34)	4.13 (3.78, 4.43)
Na (mmol/L)			
Baseline	139.9 (138.2, 140.4)	141.2 (139.2, 141.5)	139.1 (138.6, 142.2)
24 h of after administration	138.2 (137.5, 139.0)	138.9 (138.0, 141.3)	139.0 (135.2, 139.0)
Ca (mmol/L)			
Baseline	2.28 (2.24, 2.28)	2.39 (2.23, 2.46)	2.37 (2.33, 2.39)
24 h of after administration	2.21 (2.20, 2.35)	2.33 (2.29, 2.36)	2.30 (2.26, 2.39)
Mg (mmol/L)			
Baseline	0.81 (0.79, 0.89)	0.84 (0.77, 0.89)	0.82 (0.81, 0.84)
24 h of after administration	0.81 (0.78, 0.84)	0.79 (0.75, 0.82)	0.78 (0.73, 0.83)
Triglyceride (mmol/L)			
Baseline	0.86 (0.59, 1.55)	0.81 (0.53, 1.39)	0.83 (0.56, 1.08)
24 h of after administration	1.08 (0.74, 1.33)	0.94 (0.69, 1.10)	0.96 (0.66, 1.00)

Cholesterol (mmol/L)			
Baseline	4.41 (4.37, 4.54)	4.43 (4.24, 4.47)	4.38 (3.62, 4.81)
24 h of after administration	4.20 (4.08, 4.30)	4.23 (4.05, 4.29)	4.09 (3.53, 5.08)
Low density lipoprotein cholesterol (mmol/L)			
Baseline	2.59 (2.43, 2.99)	2.38 (2.30, 2.44)	2.26 (1.65, 2.69)
24 h of after administration	2.47 (2.39, 2.72)	2.28 (2.13, 2.31)	2.28 (1.73, 2.81)
High density lipoprotein cholesterol (mmol/L)			
Baseline	1.28 (1.22, 1.47)	1.59 (1.32, 1.74)	1.62 (1.16, 2.02)
24 h of after administration	1.21 (1.16, 1.28)	1.43 (1.38, 1.54)	1.48 (1.17, 1.88)
Glucose (mmol/L)			
Baseline	4.56 (4.35, 4.95)	4.52 (4.20, 4.90)	4.62 (4.39, 5.04)
24 h of after administration	4.60 (4.49, 4.79)	4.88 (4.58, 5.07)	4.98 (4.76, 5.03)
Urine routine			
Red blood cell (/uL)			
Baseline	5.00 (3.00, 9.00)	3.50 (1.00, 5.00)	4.00 (1.00, 14.00)
24 h of after administration	3.50 (2.00, 5.00)	2.50 (1.00, 5.00)	2.50 (1.00, 8.00)
White blood cell (/uL)			
Baseline	3.00 (1.00, 9.00)	4.00 (1.00, 10.00)	1.00 (0.00, 2.00)
24 h of after administration	4.50 (1.00, 7.00)	2.00 (1.00, 5.00)	1.50 (1.00, 2.00)
Troponin (ng/L)			
Baseline	4.75 (3.60, 5.90)	4.85 (3.70, 5.20)	3.55 (3.20, 3.90)
24 h of after administration	4.90 (4.00, 6.00)	4.35 (3.40, 5.40)	3.75 (3.40, 4.10)

Note: All data are presented as median (1st to 3rd) quartile.