Electronic Supplementary Material (ESI) for Journal of Materials Chemistry B

Gold Nanoparticle Conjugated PLGA-PEG-SA-PEG-PLGA Multiblock Copolymer Nanoparticles: Synthesis, Characterization, In-vivo Release of Rifampicin

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Supplementary Material

1. Green synthesis of CPEG stabilized AuNPs

The reduction of Au (III) to Au (0) is facilitated by citric acid units present in the CPEG dendron at pH 8.5. It was very interesting to monitor the rapid formation of AuNPs with the addition of CPEG dendron at 80 °C. The synthesized AuNPs were examined by UV-Visible spectral analysis and the result is shown in the Fig.S1a. The AuNPs colloidal solution shows the surface plasmon resonance (SPR) absorption at 530 nm. The TEM images in Fig.S1b indicate that AuNPs are uniformly arranged on the CPEG polymer matrix and confirm that the CPEG stabilized AuNPs are about 17 nm with spherical shape. The scheme of AuNPs synthesis using CPEG is given below.

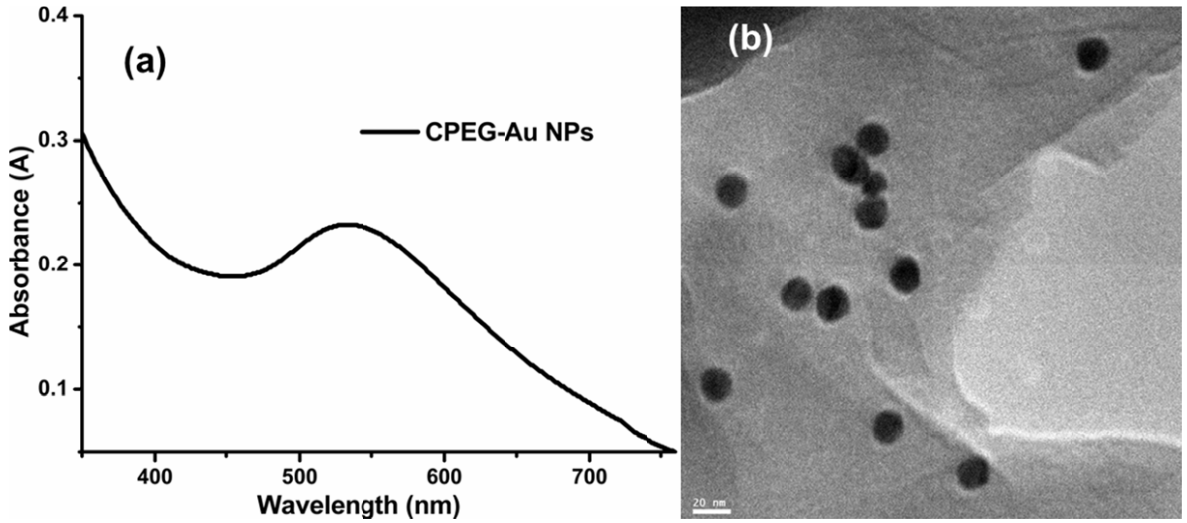
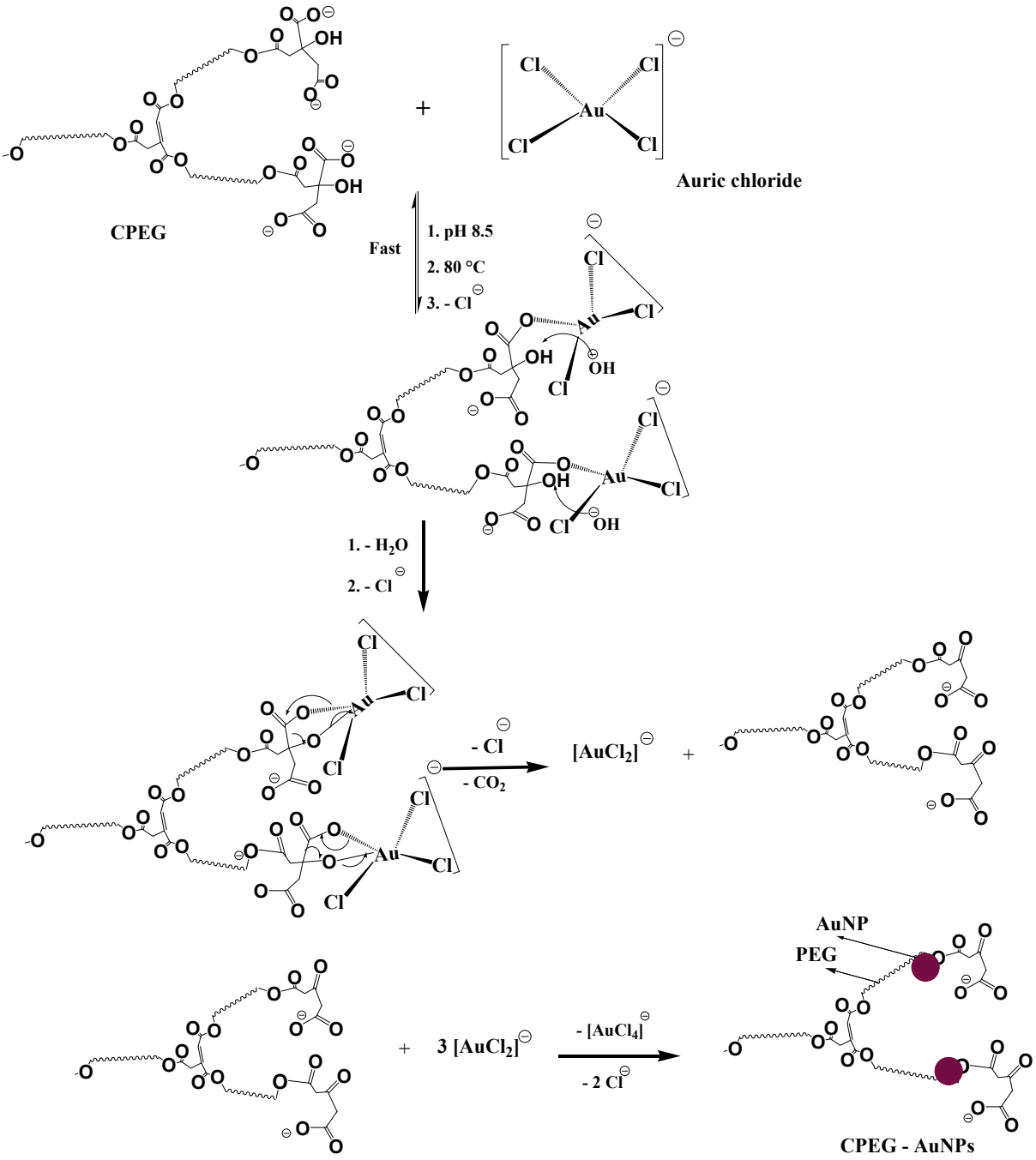


Fig. S1. (a) UV-visible spectrum and (b) TEM images of CPEG stabilized AuNPs (scale bar 20 nm).

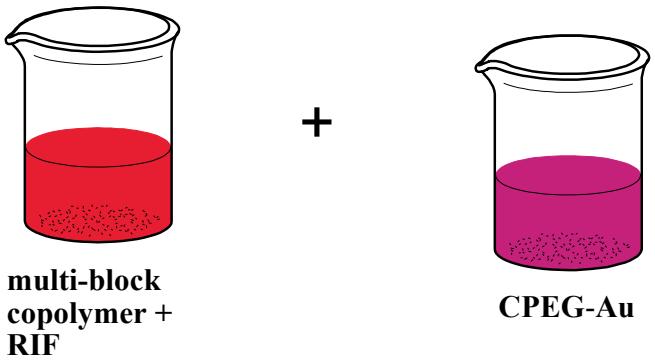


Scheme S1. Scheme of synthesis of AuNPs using CPEG.

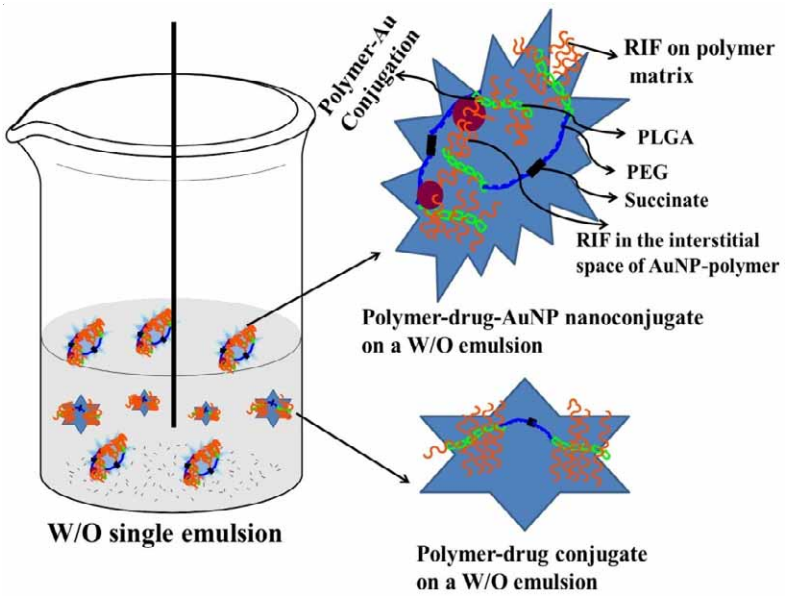
2. Scheme of RIF loaded AuNPs conjugated multiblock copolymer nanoparticles by W/O/W double emulsion technique

Step-1

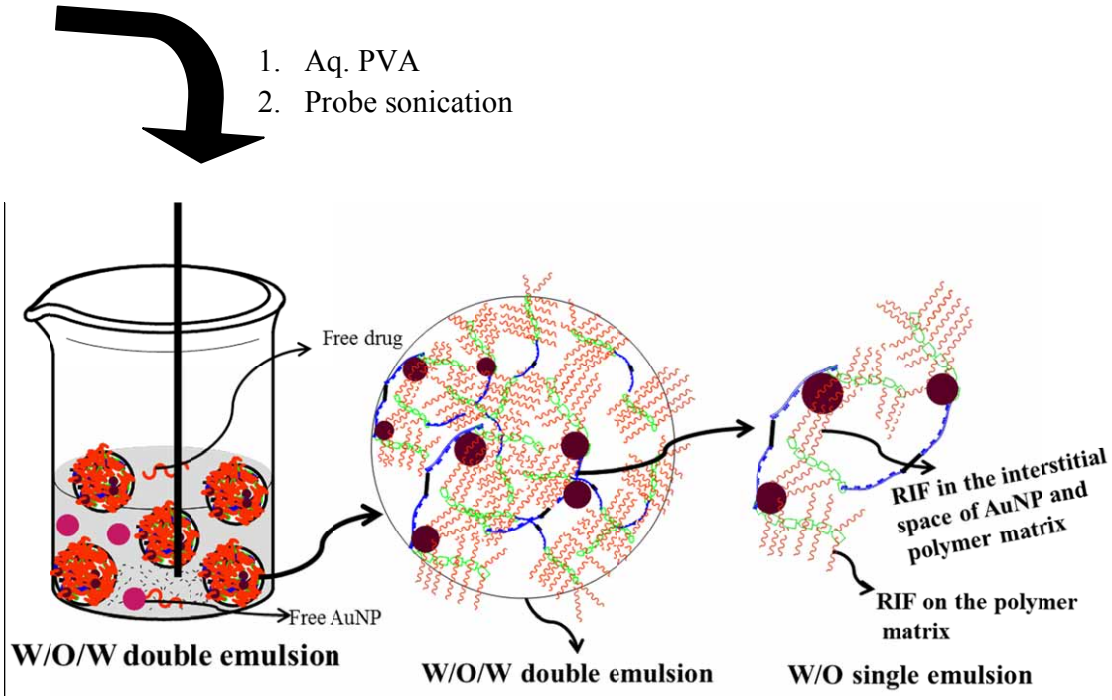
Formation of W/O single emulsion



Probe sonication



Step – 2: Formation of W/O/W double emulsion



(RIF loaded Au-polymer nanoparticle)

Scheme S2. Mechanism of preparation of RIF and AuNPs loaded polymer nanoparticles by W/O/W double emulsion technique.

During the W/O single emulsion,

The polymer-drug-AuNPs nanoconjugates and polymer-drug conjugates are formed on the small W/O emulsion droplets.

In this step,

During the probe sonication, the PEG surrounded AuNPs are detached from the CPEG-Au dendron and capped by the polymer matrix. The capping of AuNPs is favored due to the presence of PEG on AuNPs and the PEG directs the AuNPs to be capped by the multiblock copolymer.

When the multiblock copolymer is used, the capping ability of RIF and AuNPs is favored. When the pure PLGA is used, The PLGA precipitates in faster rate due to its hydrophobic nature and hence, the probability of capping the RIF and AuNPs is minimum resulting in lower drug loading efficiency.

During the W/O/W double emulsification, the small W/O single emulsion droplets form the secondary emulsion with PVA aqueous solution. In this stage, the PVA stabilizes the polymer-drug-Au nanoconjugates and polymer-drug nanoconjugates within a sphere. Hence, after the washing and vacuum dry, a spherical shape polymer NPs are obtained. The drug is present in three different environments in the Au conjugated polymer nanoparticle. In the structure of drug loaded Au-polymer NPs, three different colors have been used to indicate that the drug is present in three different environments.

Where,

Green particles denotes the drug on the surface of polymer NPs, blue particles denotes the drug inside the polymer matrix and red particles denotes the drug in the interstitial space of AuNPs and polymer matrix.

3. XPS traces of RIF loaded PLGA-AuNPs nanoconjugates

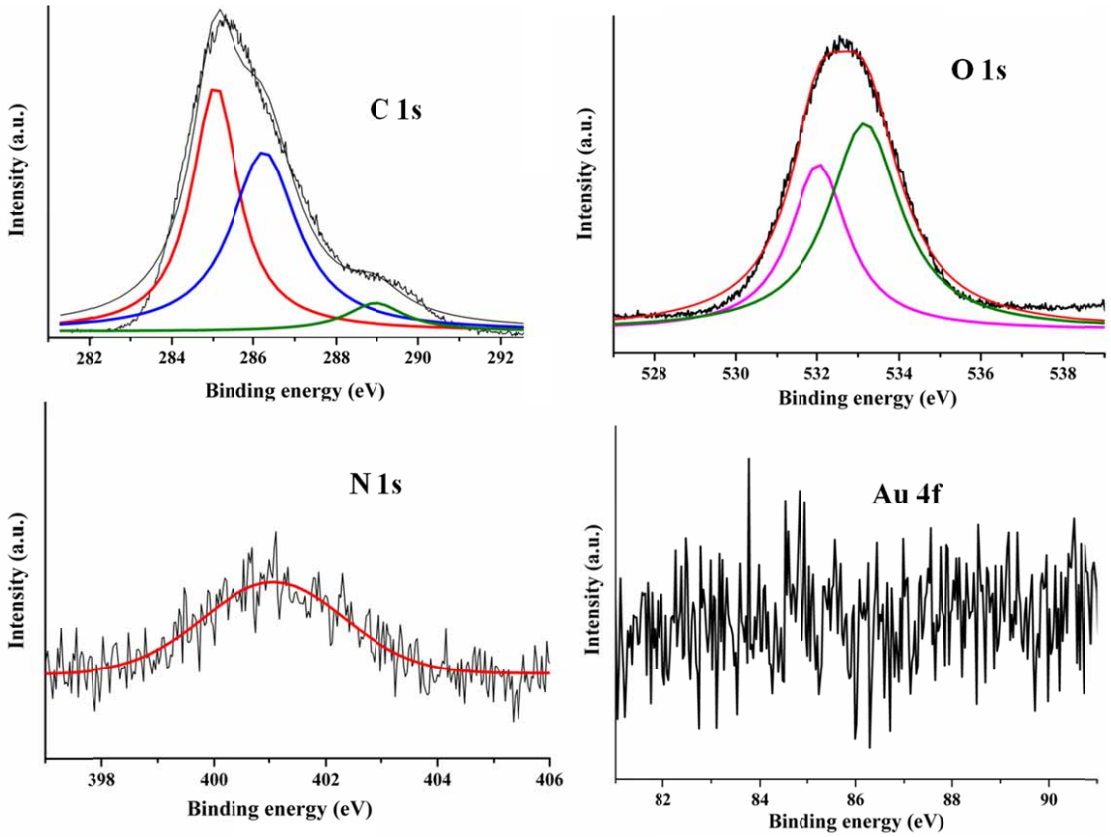


Fig. S2. XPS traces of RIF loaded PLGA-Au NPs (PSP0AuR).

4. Pharmacokinetics results of RIF metabolites

The pharmacokinetics values of DRIF, rifampicin quinone (RQ) and rifampicin N-oxide (RNO) obtained for PSPAuR series NPs are given in the Tables S1–S3 and Figs. S3–S5. The area under the curve ($AUC_{0-\infty}$) and maximum concentration (C_{max}) values of metabolites are obtained in ng.h/mL and ng/mL respectively while those of RIF are obtained in µg.h/mL and µg/mL respectively. Since, the C_{max} values obtained for the metabolites of RIF are below 25 ng/mL, the quantification of the metabolites may not be accurate. However, it is to be noted that the bioavailability of RIF is increased with lower concentration of the metabolites.

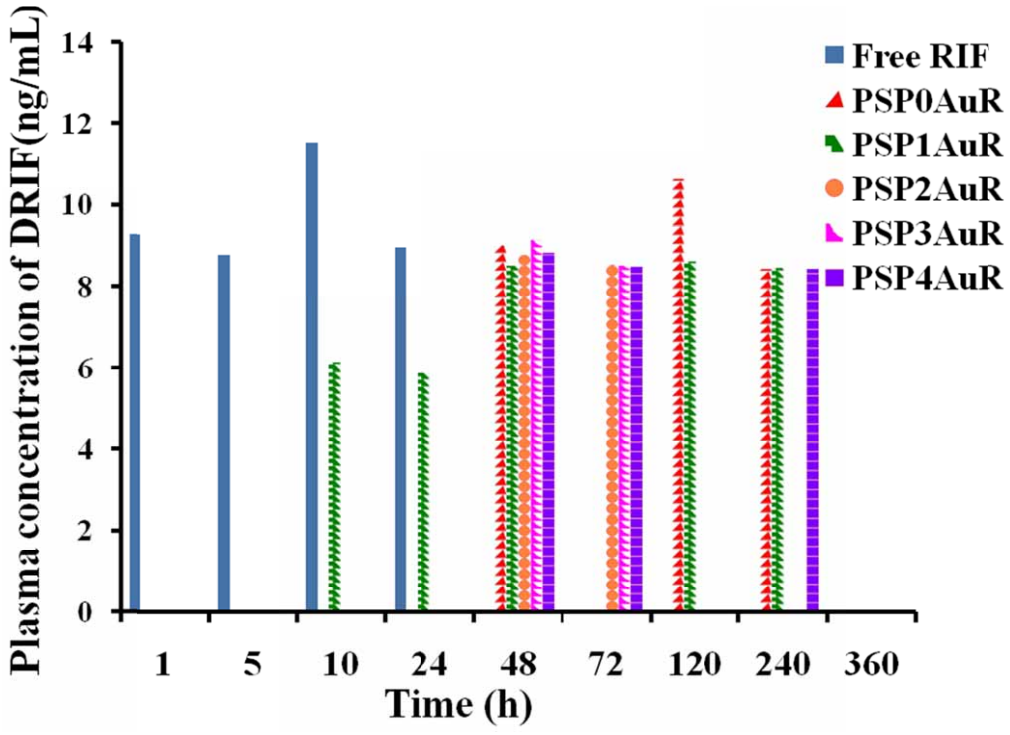


Fig. S3. Histogram of DRIF plasma concentration Vs Time profile.

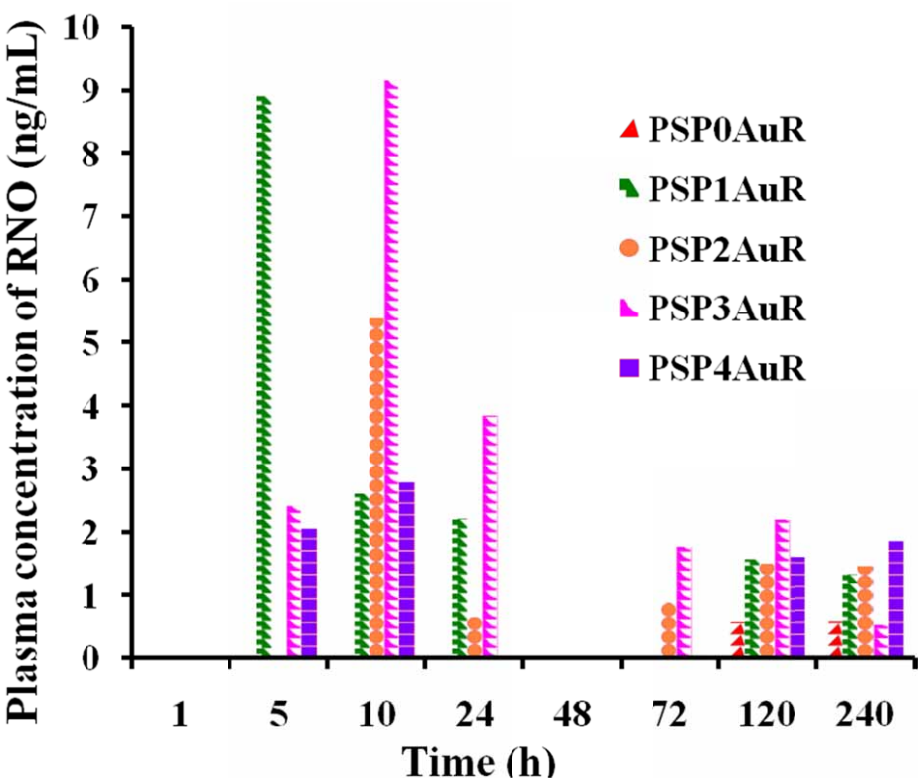


Fig. S4. Histogram of RQ plasma concentration Vs Time profile.

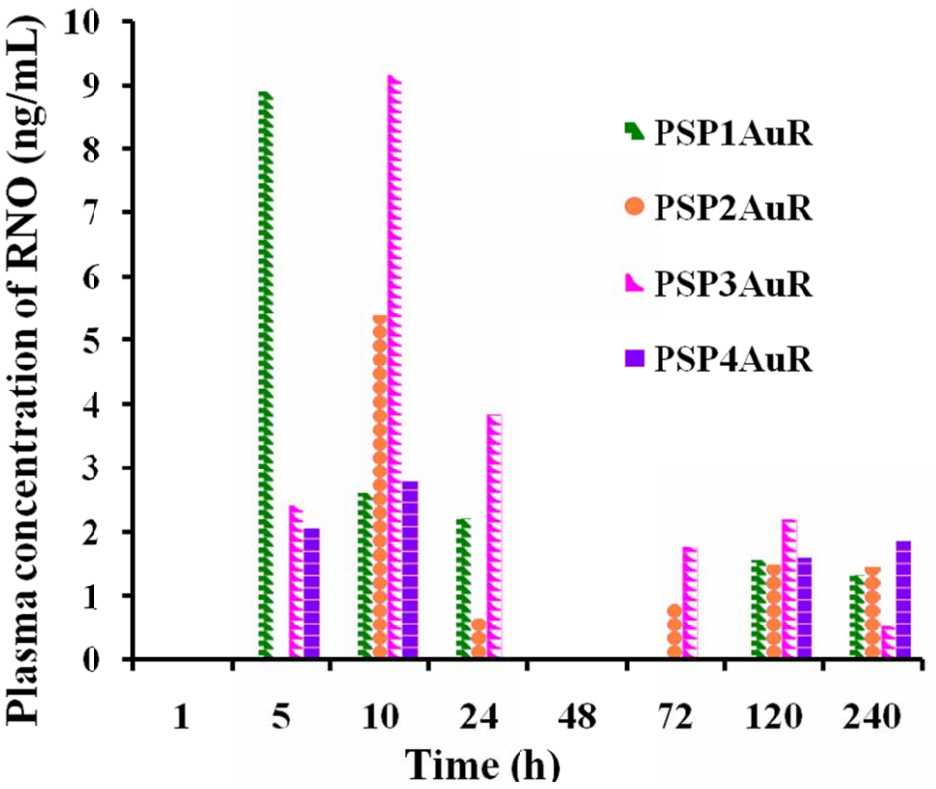


Fig. S5. Histogram of RNO plasma concentration Vs Time profile.

Table S1. Pharmacokinetics results of DRIF

samples	$AUC_{0-\infty}$ (ng.h/mL)	C_{max}(ng/mL)	T_{max}(h)	Relative bio availability	$AUC_{0-\infty DRIF}$/ $AUC_{0-\infty RIF}$
Free RIF	342	11.5	10	1	0.0182
PSPAu0	2122	10.6	120	6.2	0.0038
PSPAu1	2113	8.6	120	6.1	0.0008
PSPAu2	518.1	8.7	48	1.51	0.0001
PSPAu3	525	9.1	48	1.53	0.0002
PSPAu4	1528	8.8	48	4.4	0.0007

$AUC_{0-\infty}$ - Area under the curve

C_{max} - maximum concentration

T_{max} - Time of maximum concentration

Table S2. Pharmacokinetics results of RQ

samples	$AUC_{0-\infty}$ (ng.h/mL)	C_{max} (ng/mL)	T_{max}(h)	Relative bio availability	$AUC_{0-\infty RQ}$/ $AUC_{0-\infty RIF}$
Free RIF	2774	19.45	48	1.0	0.148
PSPAu0	2895	19.72	48	1.04	0.0052
PSPAu1	3921	17.43	24	1.41	0.0015
PSPAu2	5210	23.57	5	1.87	0.0014
PSPAu3	4092	19.00	72	1.47	0.0015
PSPAu4	3991	17.9	10	1.43	0.0019

Table S3. Pharmacokinetics results of RNO

samples	$AUC_{0-\infty}$ (ng.h/mL)	C_{max}(ng/mL)	T_{max}(h)	Relative bio availability	$AUC_{0-\infty RNO}$/ $AUC0-\infty_{RIF}$
Free RIF	0	-	-	-	-
PSPAu0	0	-	-	-	-
PSPAu1	399	8.9	5	-	0.0001
PSPAu2	396	5.3	10	-	0.0001
PSPAu3	481	9.1	10	-	0.0001
PSPAu4	392	2.7	10	-	0.0001