



## Response to comments on “Gelation of microemulsions and release behavior of sodium salicylate from gelled microemulsions”, [Eur. J. Pharm. Biopharm. 2009, 71, 297]

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We appreciate their valuable comments involving our work published in EJPB. For their four points of criticism, we would like to answer them as following:

1. We agree with their point of review that the phase behaviour and the microstructure of microemulsions strongly depend on the temperature and the composition. Indeed, no phase studies were reported in our paper. The main reason is based on a fact that the composition of our microemulsions (Table 1 in our paper) was chosen from the area of microemulsions reported in an article (H. Chen et al. Hydrogel thickened microemulsion for topical administration of drug molecule at an extremely low concentration, *Int. J. Pharm.* 2007, 341, 78–84, it is a same one given by Dr. Stubenrauch). We have cited this article as Ref. [18] in our paper.

Our paper involves very primary research on the gelation of microemulsions in the presence of gelator and release of model drug (water soluble sodium salicylate) from the system. The influence of the gelator and the sodium salicylate on the phase behaviour is not studied in our paper. We agree with the comments that it is better to study this influence. However, in our experiments, the resultant gels were homogenous and no phase separation was observed. As we mentioned in our paper, “this result can be ascribed to the cooperating effect of gelator aggregates (in oil phase) and surfactant aggregates (in aqueous phase) in the gelation of microemulsions” (the reference was also given as Ref. [21] in our paper: A. Heeres et al. Orthogonal self-assembly of low molecular weight hydrogelators and surfactants, *J. Am. Chem. Soc.* 2003, 125, 14252–14253). As shown in Fig. 1 in our paper, the gel is not transparent, we cannot clearly identify whether the system is a 1-phase microemulsion by a visual method (this should be further investigated). Obviously, the formation mechanism is different from conventional microemulsion-based organogels (MBGs),

which usually form from gelatin. Thus we use the term “gelled microemulsion”, in fact, which referred to Dr. Stubenrauch’s work (Langmuir 2007, 23, 7730). We have also cited this article in our paper as Ref. [15]. We should note that we were unable to find their two books and another article (Langmuir 2008, 24, 8473) when we prepared our paper in earlier of 2008.

Probably, we should well understand and distinguish the terms “gelled microemulsion” and “microemulsion-based gel (MBGs)”. For conventional MBGs, the continuous phase should be microemulsion. In our experiments, the microemulsion was macroscopically gelled (as shown in Fig. 1).

2. As we answer above, indeed, our system is not transparent. The gelator used in our system is an efficient gelator for the gelation of oil phase (IPM). We are not sure whether it is the best one for our system. We proposed “gelled microemulsion” mainly based on the macroscopical observation and orthogonal self-assembly of gelators and surfactants referring to an article (A. Heeres et al. *J. Am. Chem. Soc.* 2003, 125, 14252–14253 as Ref. [21] in our paper).

3. In principle, we agree with this comments regarding to the propylene glycol as co-surfactant. Considering that it is not subject to be investigated in our paper, we directly use it as a component of composition based on the literature (Ref. [18] in our paper) without further discussion in our paper.

4. This comment would be valuable for us. Fig. 6 in our paper shows schematically representation of discontinuous structure formation and the drug release from the gelled microemulsions. We just proposed a possible assumption to explain our experimental results. We agree with the comment that no general rules can be drawn for such a complicated system. We are currently unable to give experimental evidence for the assumption.

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