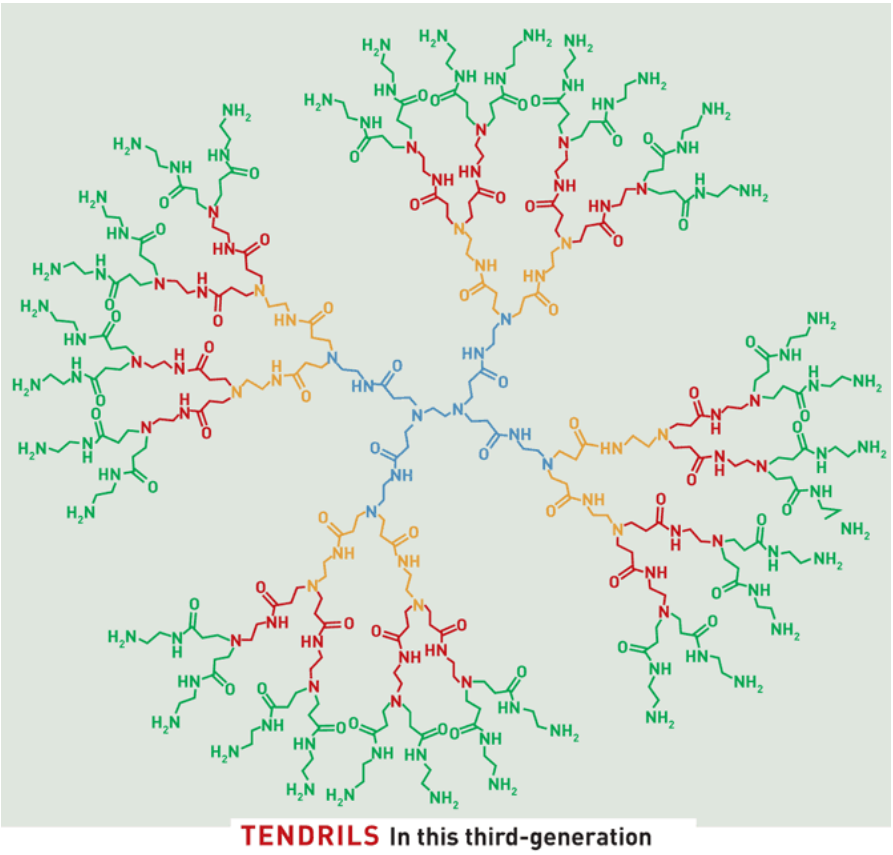
Нанохимия и функциональные наноматериалы (студенты, аспиранты, молодые ученые).
Задача 10 «Дендримеры» (базовая).

Polyamidoamine (PAMAM) dendrimers (Fig. 1) have recently attracted much attentions from biomedical researchers due to their biocompatibility and biodegradability. In one application, third generation PAMAM dendrimers were conjugated to an anti-inflammatory drug, N-Acetyl-L-Cysteine (NAC) via a crosslinker containing a disulfide bond. PAMAM-NAC conjugates were found to be highly efficient in treatment of a number of inflammatory conditions occurring in different parts of the body, including chorioamnionitis (an inflammation of fetal membranes due to a bacterial infection that can lead to cerebral palsy of the newborn), secondary spinal cord injuries, and macular degeneration.



TENDRILS In this third-generation PAMAM dendrimer, the core is shown in blue and each successive generation is shown in a different color.

Figure 1. Structure of a third generation PAMAM dendrimer.

A) What is molecular weight of the dendrimer shown in Fig. 1? (**1 pt**)
B) How would you synthesize this dendrimer? You can use any commercially available reagents. (**2 pts**)
B) Propose a synthetic route to prepare PAMAM-NAC conjugates from the PAMAM dendrimer shown in Fig.1 and NAC. You can use any commercially available crosslinker (please provide the name of the supplier and verifiable catalog number). It is important

that NAC is attached via a disulfide bond and the conjugate will release exactly the NAC molecule upon cleavage of this bond. (**2 pts**)
C) Calculate drug loading (wt. % of the drug in the conjugate) for your conjugate. (**1 pt**)
D) It was noted that injected PAMAM-NAC conjugates remain stable in the blood stream or in extracellular fluids but quickly release the drug after being internalized by cells. Explain the chemistry of this finding. (**2 pts**)
E) In order to determine the reason for universal action of PAMAM-NAC conjugates in different inflammatory conditions, researchers performed animal studies of biodistribution of the conjugates. The experiments showed that majority of the injected conjugates accumulated in the sites of inflammation, while unconjugated NAC was uniformly distributed with the body. Explain why accumulation in the sites of inflammation results in higher efficacy of PAMAM-NAC conjugates compared to the free drug. (**2 pts**)
F) Suggest a possible mechanism of targeted delivery of PAMAM-NAC conjugates to inflammatory sites. (**2 pts**)

За решение на английском языке – дополнительные **2 балла**.

Методические замечания:

1. Задача решается в рамках базовых знаний и здравого смысла

2. Вопросы можно задать в специальном разделе форума http://www.nanometer.ru/forum/viewforum.php?f=19 или найти ответ самостоятельно (в том числе изучив доступные Вам Лекции на сайте Олимпиады http://www.nanometer.ru/lectures.html?UP=156195)

3. Решение оформляется и отсылается только в электронном виде, как описано в инструкциях к работе с задачами и решениями заочного теоретического тура, приведенных в разделе «Олимпиада» http://www.nanometer.ru/olymp2_o4.html

4. Подписывать решения не надо, Ваша фамилия, имя и отчество будут зашифрованы при проверке, идентификация для системы проверки производится по логину и паролю, который Вы вводите при входе на сайт Олимпиады www.nanometer.ru в качестве участника (этот пароль Вы задавали при регистрации и заполнении анкеты участника).