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Dextran-IONPs ADME Study using SWISS ADME – in Silico Study

M. Yasser Alsedfy[1, 3*], A. A. Ebnalwaled[1] and Mona Moustafa[2], Alaa Hassan Said[1]

[1]Electronics and Nano Devices lab, Faculty of Science - South Valley University, Qena 83523 Egypt.
[2]Physics department, Faculty of science, Minia University, Egypt.
[3]Department of radiology, faculty of applied health sciences, Sphinx University, New Assiut, Egypt.
Email: muhammadyasseralhussainy@gmail.com , https://orcid.org/0000-0003-2237-7602

ABSTRACT

Dextran-coated iron oxide nanoparticles (IONPs) have been explored for various biomedical applications, including the treatment of iron deficiency anemia (IDA), in this study we introduced an in silico ADME study using swiss adme to investigate the physicochemical properties, pharmacological properties, and drug likeness of dextran coated IONPs, which shown a high molecular weight and low bioavailability and drug likeness properties.

We recommend further studies in this point in future for more clarification.

Introduction

Dextran-coated iron oxide nanoparticles (IONPs) have been explored for various biomedical applications, including the treatment of iron deficiency anemia (IDA). IDA is a condition characterized by insufficient iron levels in the body, leading to reduced hemoglobin production and impaired oxygen delivery to tissues. Traditional treatments for IDA often involve oral iron supplements or intravenous iron infusions. However, oral iron can cause gastrointestinal side effects, and intravenous iron requires medical supervision. Dextran-coated IONPs offer a promising alternative due to their potential for targeted delivery and reduced side effects [1].

The synthesis of dextran-coated IONPs typically involves coating iron oxide nanoparticles with dextran, a biocompatible polysaccharide. This coating enhances the stability and biocompatibility of the nanoparticles, allowing them to circulate in the bloodstream without being rapidly cleared by the immune system. Dextran-coated IONPs can be designed to release iron in a controlled manner, potentially improving the efficacy of iron supplementation. Additionally, these nanoparticles can be engineered to target specific tissues or cells, which might enhance their therapeutic effects while minimizing systemic side effects [2].

While dextran-coated IONPs show promise for treating IDA, further research is needed to fully explore their safety and efficacy. Studies on similar iron-based treatments, such as low molecular weight iron dextran infusions, have shown rapid improvement in iron levels with a reasonable safety profile. However, the use of nanoparticles introduces unique considerations, including potential toxicity and biodistribution issues. Therefore, comprehensive toxicological evaluations and clinical trials are essential to ensure that dextran-coated IONPs are safe and effective for treating IDA [3].

From this point we will introduce a computational model for dextran coated IONPs and study its pharmacological properties using swiss ADME tool.

Materials and methods

The model of dextran coated IONPs has been drawn using chemdraw tool , after that it saved in SDF tool to be converted into smile code for further in silico analysis.

The file was uploaded to swiss ADME server to get pharmacological properties results.

Results and discussion

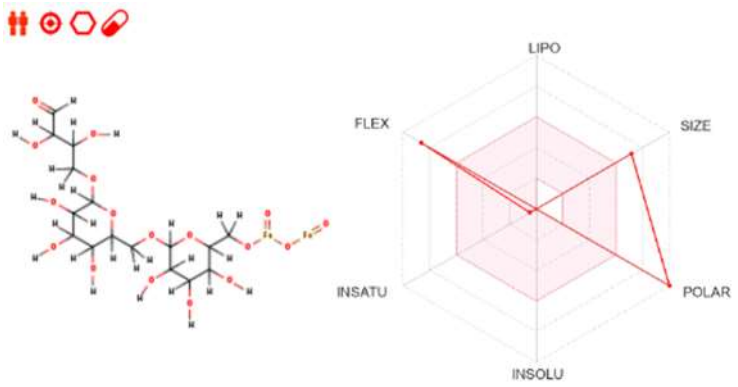

Figure 1. The model of dextran coated IONPs and its bioavailability radar

Table 1. Physicochemical properties

Compounds	MW	HA	AHA	RB	HBA	HBD	MR	TPSA
Dex-IONPs	603.07	35	0	13	17	8	91.12	268.43

Table 2. Lipophilicity characteristics

Compounds	iLOGP	XLOGP3	WLOGP	MLOGP	Silicos-IT Log P	Consensus Log P
Dex-IONPs	0	-6.52	-6.27	-8.12	-7.44	-5.67

Table 3. Water solubility characteristics

compounds	**ESOL Log S**	**ESOL Solubility (mg/ml)**	**ESOL Solubility (mol/l)**	**ESOL Class**	**Ali Log S**	**Ali Solubility (mg/ml)**	**Ali Solubility (mol/l)**	**Ali Class**
Dex-IONPs	1.39	1.47E+04	2.44E+01	Highly soluble	1.58	2.28E+04	3.78E+01	Highly soluble

Table 4. Drug pharmacokinetics

compounds	**GI absorption**	**BBB permeant**	**Pgp substrate**	**CYP1A2 inhibitor**	**CYP2C19 inhibitor**	**CYP2C9 inhibitor**	**CYP2D6 inhibitor**	**CYP3A4 inhibitor**	**log Kp (cm/s)**
Dex-IONPs	Low	No	Yes	No	No	No	No	No	-14.61

Table 5. Drug likeness

compounds	**Lipinski #violations**	**Ghose #violations**	**Veber #violations**	**Egan #violations**	**Muegge #violations**	**Bioavailability Score**
Dex-IONPs	**3**	**2**	**2**	**1**	**5**	**0.17**

From tables 1,2,3,4,5 we can get very important insights about dextran coated IONPs in the context of treating IDA, dextran-IONPs seems to have high molecular weight in our model which was 603 dalton.

A Consensus Log P value of -5.67 indicates that a substance is highly hydrophilic, which can affect its oral bioavailability. Generally, for a drug to be orally bioavailable, it should have a log P within a certain range that balances lipophilicity and hydrophilicity. The Rule of Five suggests that a clog P should ideally be between 0 and 5 for optimal oral absorption1. A log P of -5.67 is far below this range, suggesting that the substance might face challenges in crossing lipid-rich cell membranes in the gastrointestinal tract, potentially leading to poor oral absorption [4].

The various water solubility models came to support that as shown in table 3, it is categorized as high water soluble, interestingly due to the high molecular weight and log Kp (cm/s) which equals -14.61 it was categorized as low GIT absorption probability and has no ability to cross blood brain barrier.

A log Kp value of -14.61 refers to skin permeability, not oral bioavailability. This value indicates extremely low skin permeability, suggesting that the substance is poorly absorbed through the skin. However, when considering oral bioavailability, different parameters are relevant. For a drug to be orally bioavailable, it typically needs to have a log Kp value (in the context of gastrointestinal absorption) between -8 and -11. This range ensures that the drug can be effectively absorbed in the gastrointestinal tract.

As shown in table 5 our model of dex-IONPs seems to be not drug like with low bioavailability score 0.17, a bioavailability score of 0.17 typically indicates that a compound has poor oral bioavailability. This score is often used in in silico studies to predict the likelihood of a drug being absorbed effectively in the body after oral administration. Compounds with a bioavailability score closer to 1 are generally considered more likely to be orally bioavailable, while scores closer to 0 indicate poor absorption.

Finally however, some studies suggest that iron from iron oxide nanoparticles can be bioavailable when administered orally, as they can release iron in the acidic environment of the stomach, which might enhance absorption. Despite this, the specific properties of dextran-coated IONPs, such as their hydrophilicity and bioavailability score, suggest challenges in achieving high oral bioavailability without further formulation optimization [5].

In summary, while dextran-coated IONPs show promise for biomedical applications, their oral bioavailability as a drug might be limited by their chemical and physical properties. Further research is needed to optimize their formulation for oral delivery.

Conclusion

In this study after an in silico analysis for computational dextran coated IONPs model , we conclude that it may not be suitable for oral administration , and need more investigations in vivo to support this in silico results

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