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The Effect of Pharmaceutical Analgesics on Renal Failure Using Novel Nano-Composite Drugs

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Abstract

Naproxen drug–polymer nanocomposite was prepared by condensation polymerisation, as reported in the medical literature. The molecular docking of the nanocomposite drug with amino acids within the 1UPT protein inside kidney cancer cells was studied.

Biochemical changes were studied by measuring the level of urea in the blood serum according to the method mentioned in the kit, and the level of creatinine was also measured according to the method mentioned in the kit .Biochemical changes were studied by taking 15 male white rats, whose average age ranged between 11 and 12 weeks, and whose weight ranged between 120 and 150 grams. They were placed under appropriate conditions in terms of temperature, the lighting period was 12 hours a day, and they were well ventilated. They fed special fodder, and they were provided with water. The white rats used in the experiment were randomly divided into three groups. The first group was given sodium chloride as a physiological saline solution orally and was considered a control group. The second and third groups were dosed with Naproxen drug and the nanocomposites-Naproxen drug, respectively, at a concentration of 51 mg/kg for 14 days .

The results concluded that some of the effects of biochemical parameters on serological and pathological changes in the Kidney were obtained as a result of the use of loaded Naproxen drug on nano co-polymer.

KeyWords: Naproxen drug, Naproxen drug nanocomposite polymer, Molecular docking, Biochemical parameters, Renal failure.

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Introduction

Nanotechnology is one of the most promising technologies used by scientists to develop pharmaceutical innovations that transform the way medicine is practised and how many diseases are treated. Nanomedicine is starting to show signs in new and persistent ways that will improve human health and lengthen lifespan [1, 2].

One of nanomedicine's most crucial tasks is making novel medications with greater advantages and fewer adverse effects. Nanotechnology could provide new medication delivery methods in several fields, including health sciences [3].

Large molecules known as polymers are composed of numerous tiny units known as monomers [4]. There has been a great interest in the polymeric materials used to deliver drugs inside the human

body (their degradation) because of their applications in medicine, such as the use of biodegradable polymers from renewable sources, which decreases the toxicity of their therapeutic efficacy, and the usage of industrial polymers, as well as many medications' problems with limited solubility and other issues [5-7].

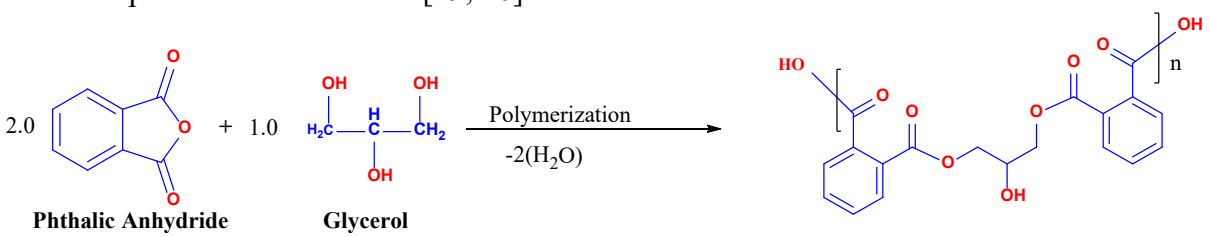
Currently, there is a need for biopolymers with a variety of characteristics unique to biological applications. Since some biopolymers elicit an immunological response in the body that can be avoided by employing an appropriate synthetic biopolymer, synthetic biopolymers offer a lot of potential in biomedical applications [8-11]. Although nanoparticles possess unique physical and chemical properties that make them useful for many industrial and medical applications, there are still some health risks and concerns due to their uncontrolled use and the toxicity associated with nanocomposites [12]. The effect of nanoparticles on human health and the environment has received very little attention. Since the primary factors influencing the toxicity of nanoparticles are thought to be their chemical makeup, particle size, shape, and surface chemistry, nanotoxicology currently lacks the knowledge essential to assess these dangers accurately [13]. The use of nanoparticles in biomedicine and other fields is accompanied by various safety issues [14-16].

Potential consequences of nanoparticles on distant organs are one area of worry. Despite the fact that this is something that nanoparticles can do, through biological barriers, it enters reproductive tissues and may harm a variety of cells. For instance, it may decrease sperm count, viability, and function, as well as interfere with fetal development [17]. Naproxen is an NSAID anti-inflammatory drug, and it is one of the most widely used therapeutic agents. Naproxen is used for non-steroidal anti-inflammatory drugs pain, such as toothache and headache. Despite its widespread use, it causes serious toxicity that includes severe gastrointestinal disorders, hepatotoxicity and renal [18].

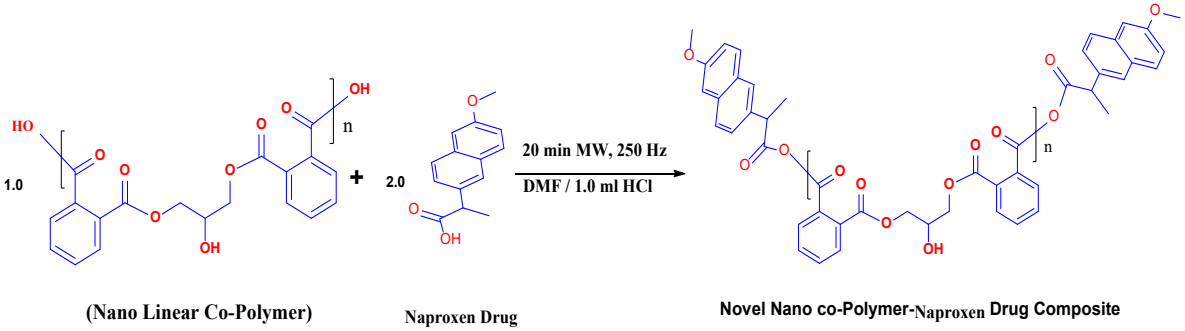
For all of the above, our current research indicates and confirms that the use of Naproxen drug nano compacts and its accumulation over time also lead to the appearance of symptoms of toxicity in the kidney tissues and thus to kidney cancer in white rats.

Materials and Working Methods

Equations 1 and 2 show that a nanopolymer-naproxen drug composite was prepared according to the method reported in the literature [19, 20].



Equation (1): Reaction of synthesis of nano-linear co-polymer



Equation (2): Reaction of synthesis of nano drug composite

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Molecular docking of the prepared nano polymer-Naproxen drug with amino acids within a protein (1upt) was studied [21].

In this experiment, the biochemical and histological changes were studied by using 15 male white rats, with an average age ranging between 11 and 12 weeks and weights ranging from 120 to 150 grams. They were placed under appropriate conditions in terms of temperature, and the lighting period was 12 hours per day. They were well ventilated, fed special fodder, and provided with water. The animals were left to acclimatise for a week.

Animals were randomly distributed into three groups equally, each group included five male rats, and the duration of the experiment was 14 days. These groups are as follows:

1. The first group consisted of (5) rats, who were given a physiological saline solution and considered a control group.
2. The second group of (5) rats that were dosed at 51 kg/mg orally for 14 days with pure Naproxen drug.
3. The third group of (5) rats that were dosed 51 kg/mg orally for 14 days with nano composite drug..

Animals were anesthetized using anesthesia (chloroform) to be anesthetized by breathing, then blood (5 ml) was withdrawn from the heart directly by stabbing the heart to obtain the largest amount of blood for biochemical tests, and then placing blood samples in test tubes free of any substance Anticoagulant and placed in a centrifuge to separate blood serum at a speed of 4000 revolutions/min for 15 minutes. The serums are kept in the refrigerator to complete the biochemical measurements.

The level of urea in blood serum was measured according to the method mentioned in the kit. Enzymatic determination of urea according to the following reaction:

$$\boldsymbol{Urea + H_2O \xrightarrow{Urease} 2NH_3 + CO_2}$$

$$\boldsymbol{2NH_3 + 2 - ketoglutarate + 2NADH \xrightarrow{GLDH} L - Glutamate + 2NAD^2 + H_2O}$$

Results And Discussion

Molecular Docking of Naproxen Drug Nanocomosites

Table 1 shows the binding energy of Naproxen drug nanocomosite with the amino acids within the (1upt) protein present in the cancer cell, as well as the lower and upper limits (RMSD). As for the **Figure 1**; showing the association of drug nanocomosite, with the amino acids contained in the protein of the cancer cell, where it is linked to the amino acid lysine (Lys), which bears the serial number (D:2180), as it is linked by a bond with the drug by a bond alkyl is pink in color. It also binds with the drug by a ketone bond, which has an orange color, in addition to that it binds with the drug with the amino acids Valine (Val), which carries the serial number (C:53) and Asparagine (Asn) which carries the serial number (C:52) which is hydrogen bonded and green in colour. As for the rest of the amino acids that appeared in light green, they bind with the protein by VanderWaals bond (Gly-Gln-Glu-Phe-Pro-Thr-Tyr-Lys-Ile-Ser-Arg).

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Table 1: Binding energy of Naproxen drug nanocomosite with the amino acids within the (1UPT) protein

Ligand	Binding Affinity (kcal/mol)	Mode	RMSD lower bound	RMSD upper bound
1upt_NOVL.cdx_uff_E=1607.39	-6.6	0	0	0
1upt_NOVL.cdx_uff_E=1607.39	-6.4	1	1.171	5.908
1upt_NOVL.cdx_uff_E=1607.39	-6.4	2	17.634	22.362
1upt_NOVL.cdx_uff_E=1607.39	-6.3	3	15.582	19.372
1upt_NOVL.cdx_uff_E=1607.39	-6.2	4	50.373	55.296
1upt_NOVL.cdx_uff_E=1607.39	-6.2	5	1.456	6.188
1upt_NOVL.cdx_uff_E=1607.39	-6.2	6	16.352	21.189
1upt_NOVL.cdx_uff_E=1607.39	-6.2	7	16.44	20.683
1upt_NOVL.cdx_uff_E=1607.39	-6.2	8	15.274	20.86
1upt_NOVL.cdx_uff_E=1607.39	-6.2	9	16.44	20.683

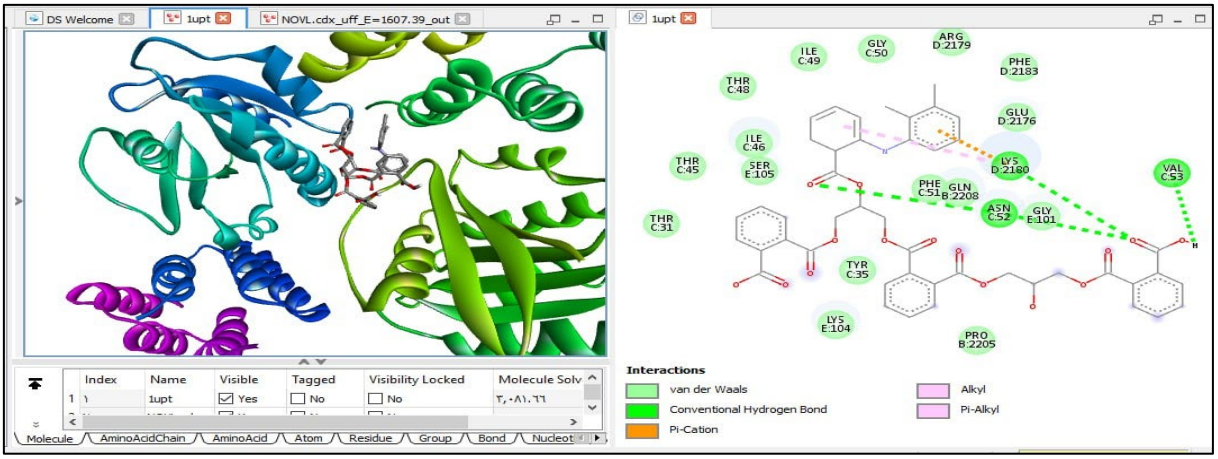

Figure 1: Association of Naproxen drug nanocomposite, with the amino acids contained in the protein (1UPT) of the cancer cell

Biological Effect Study

The results of the study showed in Table 2, that there was no significant difference in the level of urea in the group of Naproxen drug concentration of 51 Kg/mg compared to the control group. There was a significant increase ($P < 0.05$) in the group of nano polymer Naproxen composite-Naproxen compared to the control group, where a significant increase ($P<.0.05$) was found in the urea level of the nano polymer-Naproxen group compared to the Naproxen group. Also, the results of the study showed in Table 2, that there was a significant increase ($P < 0.05$) in the level of creatinine in the group of Naproxen drug concentration of 51 Kg/mg and the group of nano-Naproxen compared to the control group, and a significant increase ($P<0.05$) in the Naproxen nano polymer composite group when compared with Naproxen drug.

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Table 2: Effect of Naproxen drug and Naproxen drug nanocomposite respectively, on the levels of urea and creatinine in the blood serum of white male rats

Norm / Groups	Urea (mg/dl)	Creatinine (mg/dl)
Control	1.03 ±31.6 A	0.010 ± 0.470 A
Naproxen drug	1.01 ±37.0 **A**	0.016± 0.762 D
Naproxen drug nanocomosite	1.88 ±44.6 C	0.013± 0.838 E
L.S.D	5.60	0.066

Rate ± standard error
Different capital letters in the vertical direction indicate significant differences, P < 0.05.

Results of the current study agree with a study [22], that showed the clear effect of non-steroidal anti-inflammatory drugs in male albino rats, as they work to inhibit the formation of prostaglandins in the kidney and this works to reduce blood flow in it, which may lead to an increase in the serum level of urea and creatinine or the reason may be due to the fact that non-steroidal drugs work to retain water and salts in the kidneys and reduce urine excretion.

As for a study [23], it was shown that the cytotoxic effects of nanoparticles are caused by a large increase in reactive oxygen species ROS and depletion of antioxidant enzymes, as the treatment of mice orally with different concentrations of nanoparticles showed signs of inflammation in the liver and kidneys and DNA damage. It was proven that oxidative stress is the mechanism Responsible for the effects that appear in the cells. There may be other reasons such as the physical properties of nanoparticles such as surface charge and the nature of the surface of the particles and their solubility in water.

The current study is one of the very few studies that dealt with drug tolerance in nanopolymers and their effect on histopathological parameters, so we mention here what was collected from the sources in interpreting the obtained results.

A study indicated that non-steroidal anti-inflammatory drugs (NSAIDs) stimulate the renin-angiotensin system, leading to acute renal failure by inhibiting the formation of prostaglandins and an increase in serum urea and creatinine levels [24]. It can also be explained by the high levels of haemoglobin and keratinine in the blood serum due to the inhibition of cyclooxygenase enzymes, which impairs glomerular filtration, which is one of the causes of renal failure [25]. Naproxen causes damage to the kidneys, and repeated doses may cause severe injuries. Either light or single doses do not threaten the patient's life and have less effect on the kidney tissue. Approximately 1-5% of patients who take NSAIDs develop nephrotoxic syndromes. Miscellaneous calls for a doctor's review [26]. Fortunately for the patient, when the doctor discovers the negative effects of these drugs, he prevents the patient from taking them based on the laboratory or histological results that are available to him [27].

Among the reasons that are taken into account and that indicate the negative effects of these drugs is the presence of a type of prostaglandin 12 that can be synthesized inside the glomerulus and interstitial cells located in the medulla of the kidney, works to reduce the initial resistance of blood vessels and redistribute blood flow from the renal cortex to the nephrons, drugs Non-steroidal anti-inflammatory drugs block the production of this type of prostaglandin, which reduces blood supply to nephrons and causes acute ischemia [28].

Conclusion

From the above, our research concludes that excessive repeated use of the Naproxen drug-polymer nanocomposites leads to the accumulation of toxins in the blood, Serum, and kidneys of albino rats.

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Thus, disruption of the functioning of these two vital systems and kidney cancer will result, as shown by the results we obtained in molecular docking.

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References

1. Ayat HA, Alsafy AH, AL-Baiati MN. Study of the effective range of drug level using a novel nano co-polymer-mefenamic acid. Int J Drug Deliv Technol. 2022;12(4):1808-13.
2. Aljanabi A, et al. Modification of polyethersulfone ultrafiltration membrane using poly(terephthalic acid-co-glycerol-g-maleic anhydride) as novel pore former. Polymers. 2022;14(16):3408.
3. Abd Nusaif KMH, Nusaif KA, IJR. Association between sex hormonal and metabolic changes in female with infertility, in Al-Najaf city patients. GinPolMedProject. 2024;4(68):1-5.
4. Abdulnabi O, Alsalame H, Al-Baiati M. Studying the use of chitosan-cephalexin nano composite to induce ROS and apoptosis in colon cancer cell line HCT-29. Moroccan J Chem. 2024;12(3):1270-80.
5. Al-Ghanimi B, Abd Nusaif KI, Al-Baiati MN. Studying the use of a novel nano chitosan loaded with amoxicillin in the treatment of lung cancer cell line (A549). Moroccan J Chem. 2025;13(2):480-94.
6. Khudhair AR, Sherazi ST, Al-Baiati MN. Adsorption of methylene blue from aqueous solutions using a novel nano co-polymer. AIP Conf Proc. 2020;2290:030021.
7. Obaid MM, Al-Baiati MN. Studying the effectiveness of using a novel nano polymer as a protein delivery system. AIP Conf Proc. 2023;2414(1):050041.
8. T.H. Zeyad, Ab, Khawla I, Maryam SN, ESA. Monitoring study on the incidence of 25-OH Vitamin D deficiency in the population of Kerbala province. Egyptian J Chem. 2022;65(SI:13):1319-22.
9. Kaygusuz H, Uysal M, Adımcılar V, Erim FB. Natural alginate biopolymer montmorillonite clay composites for vitamin B2 delivery. J Bioactive Compat Polym. 2015;30(1):48-56.
10. Abd Nusaif KI, Al-Baiati MN, Abbas AH, Abed AS, Abood ES. Nano-poly chitosan-ampicillin drug: synthesis, characterization and cytotoxicity. Egyptian J Chem. 2022;65(131):1313-8.
11. Abbas AH, Al-Baiati MN. Use of nano-poly chitosan cephalexin drug to inhibit spread of cancer cells. Int J Drug Deliv Technol. 2023;13(1):29-32.
12. Bahadar H, Maqbool F, Niaz K, Abdollahi M. Toxicity of nanoparticles and an overview of current experimental models. Iran Biomed J. 2016;20(1):1-11.
13. Johnston HJ, Hutchison G, Christensen FM, Peters, Hankin S, Stone V. A review of the in vivo and in vitro toxicity of gold particulates, particle attributes and biological mechanisms responsible for the observed toxicity. Crit Rev Toxicol. 2010;40:328-46.
14. Kumar A, Vemula PK, Ajayan PM, John G. Silver-nanoparticle-embedded antimicrobial paints based on vegetable oil. Nat Mater. 2008;7:236-41.
15. Sung JH, Ji JH, Yoon JU, Kim DS, Song MY, Jeong J. Lung function changes in Sprague Dawley rats after prolonged inhalation exposure to nanoparticles. Inhal Toxicol. 2008;20:567-74.
16. Ali HA, Abd KI. Identifying the LBP and insulin resistance: potential role for the increased feto-maternal morbidity and long-term complications. Biochem Cell Arch. 2020;20(2):5781-6.

17. Ema M, Kobayashi N, Naya M, Hanai S, Nakanishi J. Reproductive and developmental toxicity studies of manufactured nanomaterials. Reprod Toxicol. 2010;30:343-52.
18. Zadeh AR, et al. Mechanism and adverse effects of multiple sclerosis drugs: a review article. Part 2. Int J Physiol Pathophysiol Pharmacol. 2019;11(4):105.
19. Shakir ZM, Kareem MM, Al-Baiati MN. Study the effects of some nano graft co-polymer-drugs on the spread of breast cancer. AIP Conf Proc. 2023;2414(1):050005.
20. Abdulridha AA, Abdul-Rida NA, AL-Baiati MN. Synthesis of novel nano co-polymer as pH sensitive drug delivery system, experimental and theoretical study. AIP Conf Proc. 2023;2414(1):050028.
21. Surur FH, Zeyad TH, AL-Baiati MN. Synthesis and characterization of novel nano co-polymer-drugs composites and using it as treatment for liver cancer. Moroccan J Chem. 2025;13(1):106-21.
22. Somchit MN, Sanat F, Hui GE, Wahab SI, Ahmad Z. Mefenamic acid induced nephrotoxicity: an animal model. Adv Pharm Bull. 2014;4(4):401.
23. Shrivastava A, Gupta A, Girshick R. Training region-based object detectors with online hard example mining. In Proceedings of the IEEE conference on computer vision and pattern recognition 2016 (pp. 761-769).
24. Ulinski T, Guigonis V, Dunan O, Bensman A. Acute renal failure after treatment with non-steroidal anti-inflammatory drugs. Eur J Pediatr. 2004;163(3):148-50.
25. Al-Aama ZMA, AL-Masoudi HQ, Abdulridha AA, Abd Nusaif KI, AL-Baiati MN. Synthesis of a smart nano graft co-polymer as drug delivery. AIP Conf Proc. 2023;2414(1):050030.
26. Whelton A, Watson AJ. Nonsteroidal anti-inflammatory drugs: effects on kidney function. In: Clinical Nephrotoxins. 1998. p. 203-16.
27. Puppala N, Reddy GA. Review on effects of NSAIDs on different systems. Asian J Pharm Res Dev. 2020;8(1):100-9.
28. Cunningham K, Candelario DM, Angelo LB. Nonsteroidal anti-inflammatory drugs: updates on dosage formulations and adverse effects. Orthop Nurs. 2020;39(6):408-13.