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Design and Evaluation of Chitosan Nanoparticles as Novel Drug Carriers for the Delivery of Gamma Oryzanol

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ABSTRACT

Background: Gamma oryzanol has been studied for its potential health benefits, including its use in managing arthritis and other inflammatory conditions. Chitosan, a biopolymer derived from chitin, has gained significant attention in the field of drug delivery and biomedical applications due its unique properties biocompatibility, biodegradability, and low toxicity.
Objective: The aim of this research was to prepare and analyse gamma oryzanol nanoparticle by using chitosan biopolymer.
Material & Method: Chitosan was taken as biopolymer in order to make nanoparticle by using ion gelation method. Gamma oryzanol loaded nanoparticles were subjected to evaluation for particle size analysis, XRD, % entrapment efficiency, drug content encapsulation efficiency, and % drug diffusion.
Result & Discussion: Prepared Gamma oryzanol nanoparticles were showed particle size in the range of (116.8) to (227.5) d-nm, less intensity of the diffraction peak when compared to that of gamma oryzanol, drug content in the range 38.67% to 73.19% (w/w), encapsulation efficiency in the rage of 46.58% to 71.31%. Percentage of drug Released after 6 h ranged from 70.14% to 93.79%. Among all the formulation, F9 was found to be optimized formulation in all the aspects.

Keywords: Gamma oryzanol, Nanoparticle, Chitosan, Biopolymer.

INTRODUCTION

Chitosan, a biopolymer derived from chitin, has gained significant attention in the field of drug delivery and biomedical applications due to its unique properties such as biocompatibility, biodegradability, and low toxicity. Chitosan nanoparticles, which are nanoscale particles made from chitosan, have emerged as a promising platform for the encapsulation, delivery, and controlled release of various therapeutic agents. This paper presents an overview of the synthesis methods, characterization techniques, and diverse applications of chitosan nanoparticles in drug delivery and biomedical fields [1]. Chitosan, obtained from the deacetylation of chitin, possesses desirable properties for biomedical applications. Its cationic nature allows interactions with negatively charged molecules, making it suitable for drug encapsulation and delivery. Chitosan nanoparticles can be prepared through techniques such as ionotropic gelation, emulsion cross-linking, and self-assembly [2]. These nanoparticles offer a high surface area-to-volume ratio and can be functionalized to enhance their targeting capabilities. Various methods are available for synthesizing chitosan nanoparticles, each influencing their size, shape, and drug-loading capacity. Common techniques include solvent evaporation, coacervation, and microfluidics. Characterization techniques such as dynamic light scattering

(DLS), transmission electron microscopy (TEM), and Fourier-transform infrared spectroscopy (FTIR) are used to assess particle size, morphology, and structural features. Chitosan nanoparticles find application in diverse areas such as drug delivery, gene delivery, imaging, and tissue engineering. Their mucoadhesive properties make them suitable for oral and nasal drug delivery. Surface modification with ligands or antibodies enables targeted drug delivery to specific cells or tissues. Chitosan nanoparticles have also been explored for crossing the blood-brain barrier to treat neurological disorders [3]. Despite their potential, challenges such as batch-to-batch variability and stability issues need to be addressed. Further research is needed to optimize the synthesis methods and understand the influence of particle characteristics on biological interactions. Continued exploration of chitosan nanoparticles' potential in personalized medicine, regenerative therapies, and combination therapy strategies is anticipated. Gamma oryzanol is a naturally occurring mixture of antioxidant compounds found in rice bran oil. It is derived from rice bran, the outer layer of rice grains that is removed during the milling process to produce white rice. Gamma oryzanol has been studied for its potential health benefits, including its use in managing arthritis and other inflammatory conditions. Potential role of gamma oryzanol in arthritis Anti-Inflammatory Properties: Gamma oryzanol has been investigated for its anti-inflammatory effects. Inflammatory responses play a key role in various forms of arthritis, including rheumatoid arthritis and osteoarthritis. The antioxidant properties of gamma oryzanol may help reduce oxidative stress and inflammation in the body, potentially offering benefits for individuals with arthritis [4].

MATERIAL AND METHODS

Chitosan was purchased from yarrow chem Gujarat Gamma oryzanol was purchased from Central Drug House New Delhi. Sodium tripolyphosphate was purchased from yarrow chem dyes Gujarat. Other required chemicals of analytical grade were procured. All the materials and chemicals of analytical grade were used.

Formulation of Gamma oryzanol nanoparticle

According to the method described by Caalvo et al. [6] that was centred on the ionised gelation of chitosan using sodium tripolyphosphate (TPP) anions, nanoparticles were created. In order to prevent aggregation, Tween80 (0.5% v/v) was used as a suspending agent throughout the ambient temperature preparation of chitosan nanoparticles. As per Table 1, the necessary amount of chitosan was extracted and dispersed into 5 ml of lactic acid while being stirred at 1020 rpm for 9.99 min. A 0.5% v/v Tween80 liquid (0.5 ml Tween-80 in 100 ml double-distilled water) was used to dissolve 50 mg of the medication in 85 ml. Following the addition of the drug solution, the chitosan solution was agitated with a magnetic stirrer for 20 minutes at 1000 rpm. In 10 ml, sodium TPP was dissolved.

Table 1: Formulation table for different batches.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Gamma oryzanol	300	300	300	300	300	300	300	300	300
Chitosan	50	75	100	50	75	100	50	75	100
TPP	25	25	25	50	50	50	100	100	100

Characterization of nanoparticles:

Particle Size determination

At CRL, Karunya University, and Coimbatore, the dimension of nanoparticles was measured using a Zetasizer. As previously mentioned, [7], the diameter of the particles was assessed after the suspension was put into the sample container.

Morphology of particles

(SEM) was used to test the particle's morphology. Using double-sided sticky tape, the formulation was held on a SEM stub for 6 minutes while being sputtered at 50 mA. To capture digital pictures of the nanoparticle, a SEM equipped with an additional electron detector was employed [9].

X-ray diffraction study

At Chandigarh University in Chandigarh, X-ray diffraction examination was achieved using an XRD-6000 diffractometer (Shimadziu, Japan). The formulation and the pure drug's crystallinity were found using X-ray diffraction examination. In a sample container made of aluminium, the powder was put. 30 mA and 40 kV were used to produce Cu radiation. As previously mentioned, [8], samples were imaged at angles of 10° to 90° at a rate of scanning of 10° min-1.

Gamma oryzanol entrapment efficiency

Centrifuging prepared nanoparticle suspensions at 1998 rpm for 31 min. The supernatant was placid, and the particles were then centrifuged once more after being cleaned with water. The UV-Visible Spectrophotometer at 327 nm was used to quantify the quantity of free Gamma oryzanol present in the supernatant [10].

The equation was used to determine donepezil's trapping effectiveness.

Drug Content determination

25 mg of the produced nanoparticles were balanced, dissolved in five millilitres of lactic acid, and then diluted to a volume of twenty-five millilitres using phosphate buffer (pH 7.4). One millilitre of the aliquots was collected, diluted with buffer to make ten millilitres, and the absorbance measured using ultraviolet-visible spectroscopy at 326 nm [10]. The overall number of drugs in the batches was determined from the absorbance.

Invitro drug release

The technique described by Ansaari et al. [11] was used to conduct permeation research using egg membrane. For two hours, concentrated HCl was left on the egg shell. Diffusion cell was adhered to the separating membrane. In the diffusion cell, 20 mg of the medication was added together with 10 ml of pH 7.4 phosphate buffer. In a 100 ml beaker, 50 ml of pH 7.4 phosphate buffer was auxiliary to the receptor compartment. After that, the assembly was fastened to the magnetic stirrer. For 6 hours, samples were taken out at predetermined intervals and analysed using a UV-visible spectrophotometer set at 327 nm.

RESULTS

Particle size analysis

Zetasizer was used to measure the dimension of chitosan nanoparticles that contained gamma oryzanol. As indicated in Table 2, the Z-average diameter of the particles (d.nm) of the chitosan nanoparticle formulations varied from (117.95) to (228.47). There are significant in vivo therapeutic uses for nanoparticles' capacity to change the biodistribution and pharmacokinetics of medicines. The measurement and surface characteristics of nanoparticles are crucial in this regard. Kupffer cells and other phagocytic cell types may easily engulf 100 nm nanoparticles, which limits their bioavailability. Blood circulates more slowly for particles with hydrophilic surfaces of 100 nm [15]. Such technologies boost the targeting effectiveness to certain areas while also extending the duration of pharmacological action [16].

Figure 1 depicts the particle size distribution chart for formulation (F- 9) (size distribution by intensity). Except for formulations F-5 and F-6, all formulations exhibited a consistent particle dimension distribution.

Table 2: Particle size distribution of Gammaoryzanol loaded chitosan nanoparticles.

Formulation Code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Z- Average (d. nm)	126.5	148.6	159.8	127.8	185.2	115.8	148.7	146.2	147.5

XRD analysis

Figures 1 and 2 display the XRD patterns of the drug alone and the chosen formulation. For gammaoryzanol, distinctive diffraction peaks were seen. However, as compared to the diffraction peak of gammaoryzanol, the nanofor- mulation was characterised by lower intensity.

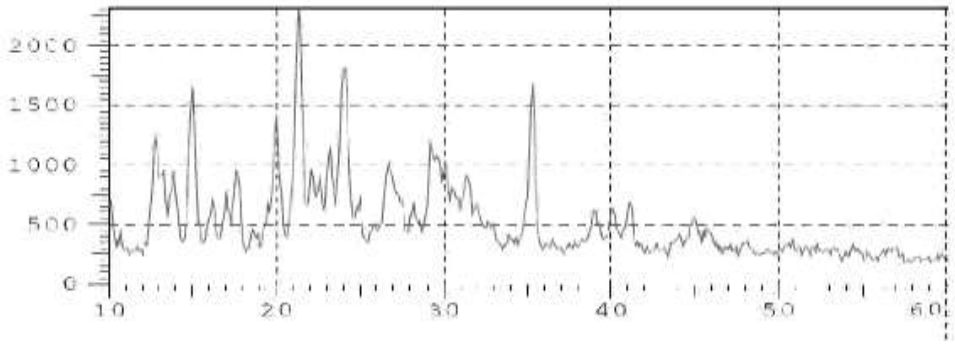

Fig. 1: XRD graph of pure drug .

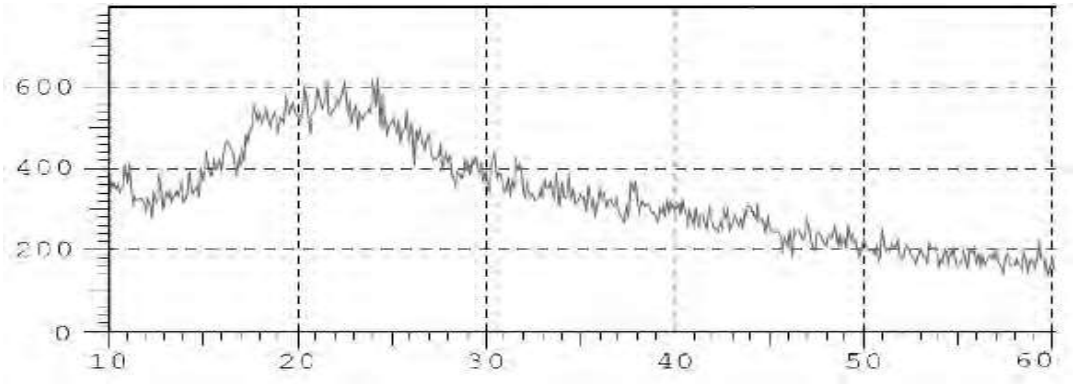

Fig. 2: X-ray diffraction of Gamma oryznol nanoparticles of F9.

SEM Analysis

SEM was used to analyse the particle morphology. Each particle unit had a nanostructure, as seen by the SEM picture (Figure 3).

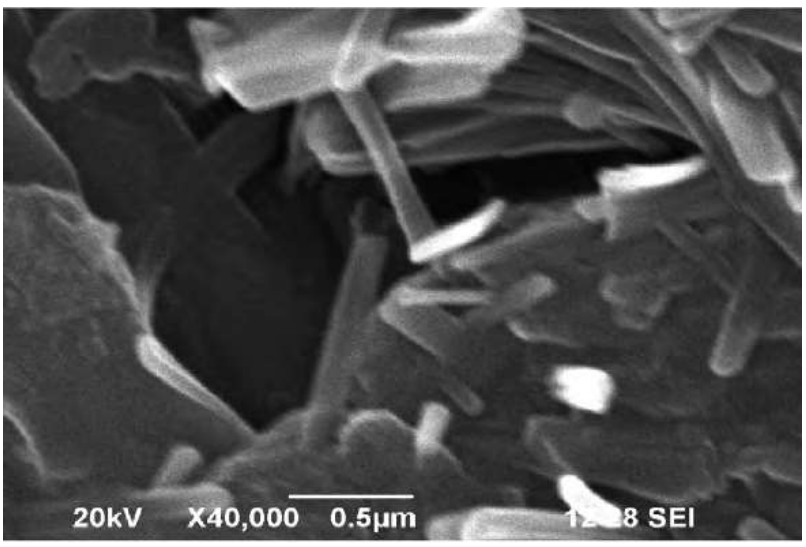

Fig. 3: Scanning Electron microscope image of Gamma oryzanol nanoparticles.

Determination of drug content and encapsulation efficiency

Ionic gelation and sonication were used to create nanoparticles of gamma oryzanol. The statistics in Table 3 make it abundantly obvious that the formulations' tested drug content fell between an array of 37.59% to 78.19% (w/w). According to Fig. 4, the encapsulation effectiveness of nanoparticle formulations ranged from 46.58% to 71.31%.

Table 3: Drug content and effective encapsulation.

Formulation	Drug Content		Encapsulation efficiency (%)
	Amount (mg)	% of 25 mg nanoparticles	
F1	11.57	45.72	54.89
F2	13.24	54.21	66.85
F3	11.43	47.65	61.24
F4	10.24	40.12	49.25
F5	17.02	68.12	68.95
F6	11.21	43.12	48.37
F7	10.85	48.25	60.12
F8	13.21	49.25	61.85
F9	17.96	73.86	82.41

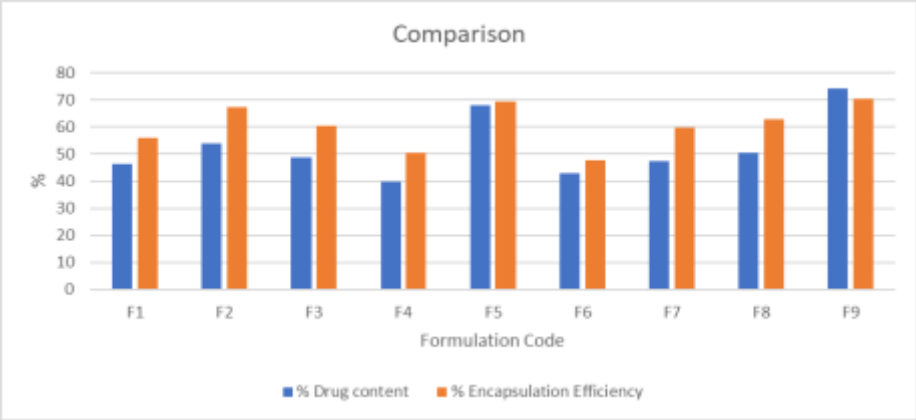

Fig. 4: Comparison of % drug content and % encapsulation efficiency.

In vitro drug release studies

Studies of natural membrane permeability (egg membrane) were conducted in accordance with the methodology described by Ansaari et al. [11]. Table 4 presents the study's findings. Figures 6 to 8 display the drug discharge profiles from the nanoparticles. The formulations demonstrated effective release of medications from the polymer, with a range of 70.14% to 93.79% for drug release after 6 hours. Entirely of the formulations' in vitro release of drugs patterns demonstrated an early burst effect followed by a gradual drug release. The burst effect happened within an hour, and the remaining medication was delivered gradually over a six-hour period.

Drug molecules that were near to the nanoparticle interface and easily diffused during the early incubation time were linked to the drug's burst release [17].

Table 4: Cumulative % drug release

Time (Hr)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
1	**20.56**	**18.39**	**24.15**	**17.25**	**20.14**	**24.51**	**21.05**	**26.98**	**33.75**
2	**37.57**	**30.14**	**35.87**	**24.36**	**33.75**	**29.95**	**35.28**	**4.21**	**40.31**
3	**54.75**	**43.95**	**42.35**	**39.24**	**50.12**	**37.14**	**52.42**	**48.35**	**51.98**
4	**60.23**	**63.02**	**67.86**	**50.34**	**60.42**	**52.637**	**66.42**	**64.89**	**70.98**
5	**68.78**	**65.78**	**78.98**	**62.59**	**72.56**	**61.23**	**75.68**	**80.98**	**8.95**
6	**86.21**	**80.54**	**85.68**	**70.23**	**86.24**	**78.21**	**88.97**	**92.01**	**94.23**

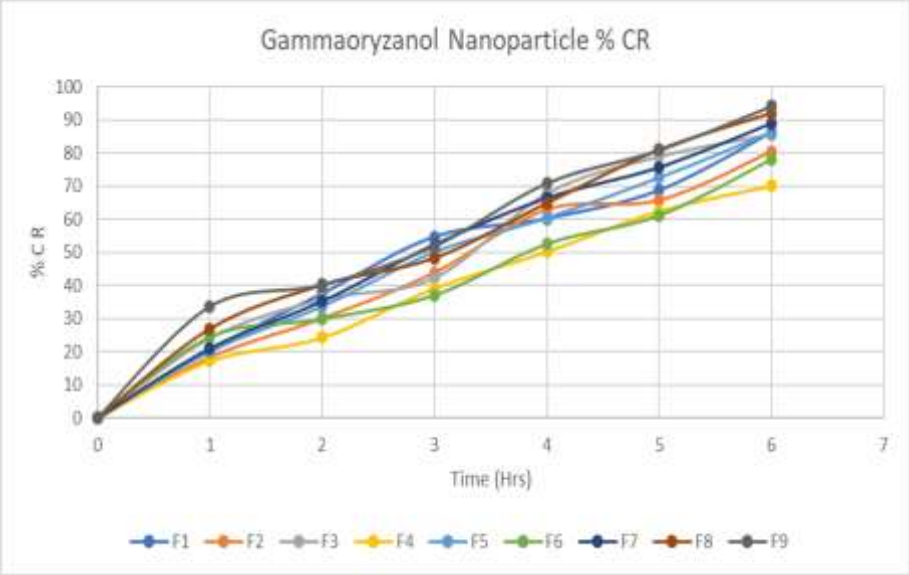

Fig. 3: % Cumulative drug release of Gamma oryzanol Nanoparticle % CR.

FTIR was used to investigate any chemical interactions between the medication and polymer under storage conditions (Fig. 9–11). After three months of holding at room temperature, no appreciable changes in the IR spectra of the drug's pure form and drug-loaded nanoparticles (F-9) were seen.

DISCUSSION

Ionic gelation, which uses TPP as a cross-linking agent, was utilised to create the donepezil nanoparticles that include chitosan, and then sonication was used to lower the particle size.

Chitosan nanoparticle compositions' Z-average particle sizes varied from 115.99 to 228.45 nm. All formulations had homogeneous particle size distribution, with the exception of formulations (F-5, F-6), which may have been because the cross-linking agent was added to the polymer at a lower concentration; the ratio of chitosan to TPP in these formulations was 3:1 and 4:1, respectively. The decrease in crystallanity of donepezil in nanomaterials as compared to the pure medication was verified by XRD analysis. Scanning electron microscopy was used to analyse the particle morphology. Each individual particle unit had a nanostructure, as seen by the SEM photograph.

In terms of drug content and encapsulation effectiveness, nanoparticle formulations performed well. This shows that the formulation procedure was appropriate and repeatable in nature, and it provided a satisfactory yield. The formulation (F-9) had the highest medication content and encapsulation efficiency. It was discovered that the percentage of encapsulation efficiency rose along with the quantity of chitosan and TPP.

According to the procedure described, permeation tests using a natural barrier (egg membrane) were conducted. The in vitro release of drugs characteristics of all the preparations revealed an early burst effect, followed by a gradual drug release. The formulations demonstrated excellent medication release from the polymer. Drug molecules that easily diffuse during the early incubation time disperse near to the tiny particles surface, which is related with the sudden release of the drug. The nanoparticles with larger drug contents released gamma oryzanol more quickly.

Additionally investigated were the drug's chemical interactions and stability within the nanoparticles. The physical and chemical properties of the formulation did not alter significantly. FT-IR was used to investigate any chemical interactions between the medication and polymer during storage. The IR spectrum of the drug-only and drug-loaded nanoparticles showed no discernible differences (Fig. 5). These

findings showed that the chitosan nanoparticles were generated are chemically as well as physically robust and maintain their medicinal qualities over a period of three months in a variety of environmental settings.

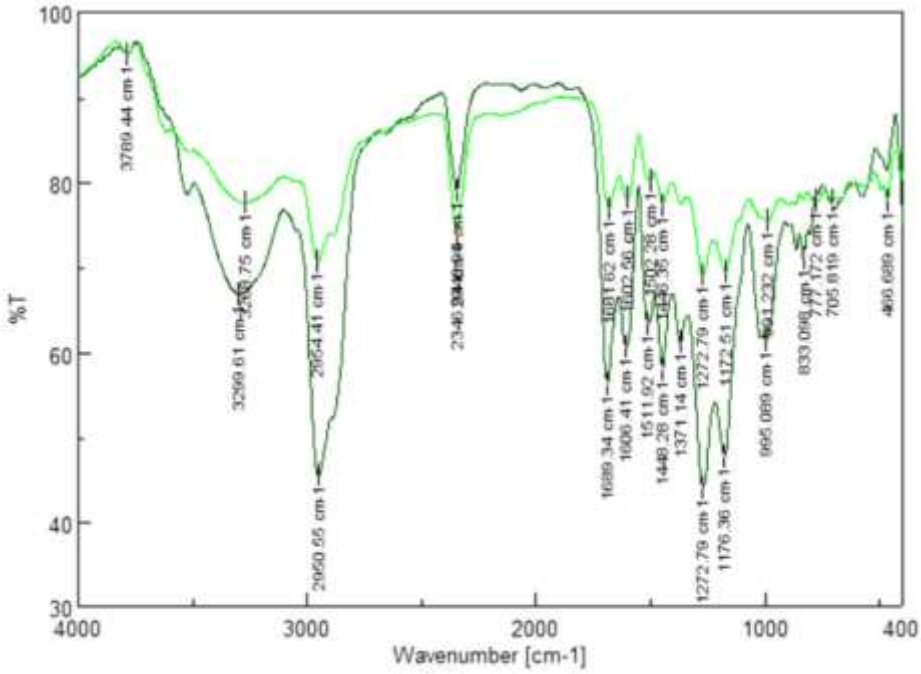

Fig. 5: FTIR spectra of Gammaoryzanol and its mixture with chitosan.

Numerous research has discussed the potential applications of nanoparticles in the treatment of arthritis. According to the results of the current investigation, gamma-oryzanol nanoparticles may be prepared using an efficient method that increases bioavailability and targets delivery for the treatment of arthritis: ionic gelation followed by sonication. It is possible to do more research using animal models to demonstrate the efficacy of made-up nanoparticles in vivo.

CONCLUSION

In this work, we created a polymeric nanocarrier that will with enhanced antiarthritic action by encapsulating gamma-oryzanol inside chitosan-TPP nanoparticles. Particle size of the improved nanoparticle formulation was 147.5 2.6 nm, which is well within the targeted range (100-200 nm). In terms of drug content and encapsulation effectiveness, nanoparticle formulations performed well. This shows that the formulation procedure was appropriate and repeatable in nature, and it provided a satisfactory yield. The formulation (F-9) had the highest medication content and encapsulation efficiency. It was discovered that the percentage of encapsulation efficiency rose along with the amount of chitosan and TPP. According to the results of the current investigation, gamma-oryzanol nanoparticles may be prepared using an efficient method that increases bioavailability and targets delivery for the treatment of arthritis: ionic gelation followed by sonication. It is possible to do more research using animal models to demonstrate the efficiency of created nanoparticles in vivo.

Declaration by Authors

Ethical Approval: Approved
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Conflict of Interest: The authors declare no conflict of interest.

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