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# Could Curcumin Gd-AuNP (Cur-Gd-AuNP) be Suitable as a Photosensitizer for Photodynamic Therapy in Alzheimer's Disease?

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**Abstract:** Alzheimer's disease (AD) is a neurodegenerative disorder that is a common form of dementia for the elderly. According to the world health organization (WHO), around 55 million older adults have dementia globally. The current medication for Alzheimer's disease is a human antibody or immunotherapy, which helps to reduce beta-amyloid plaques. However, this cures the symptom but not the disease. Photodynamic therapy (PDT) might be a good choice for AD because it is non-pharmacological. With a few side effects only, especially in the usage of natural traditional Chinese medicine combined with nanotechnology, "curcumin" as a photosensitizer (PS), that enhances the efficacy of PDT. This short communication discusses the synthesis of curcumin Gd-AuNP (Cur-Gd-AuNP) and describes its application for PDT to treat AD in future development.

**Keywords:** Alzheimer's disease; photodynamic therapy; curcumin.



## 1. Introduction

Photodynamic therapy (PDT) has been used in the medical field such a long time and has been approved by the Food and drug administration (FDA). The brief principle of PDT involved three major components: a light source, a photosensitizer (PS), and tissue oxygen. When the PS is activated with a suitable wavelength, it generates the reactive oxygen species (ROS) to cause cell damage and death for the corresponding disease [1-5]. The most common PS is porphyrin [6-9], phenothiazine [10-13], and cyanine [14-16], usually with a wavelength from 600-800 nm for photo-activation, but these are not natural PS. Chinese medicine photosensitizer is a pure compound lacking toxicity and selectively binds to the target region [17]. Curcumin possesses a variety of biological activities such as antiviral [18], antioxidant [19], anti-inflammatory [20], anticancer [21], antimicrobial [22], neuroprotective [23], cardioprotective [24], and radioprotective effects [25]. Besides, it is favorable to promote bone movement and bone-strengthening for preventing osteoporosis [26]. However, curcumin has some serious limitations, including poor water solubility, instability, and scarce bioavailability [27]. It requires the help of nanotechnology to improve and enhance its solubility, stability, and bioavailability [28, 29]. The metal, Gadolinium (Gd), is a contrast agent in the nanoparticle with good biocompatibility, low toxicity, and prolonged circulation time for imaging in the

brain [9, 10]. Thus, there is a new strategy to synthesize curcumin Gd-AuNP (Cur-Gd-AuNP) for photodynamic therapy in treating Alzheimer's disease [30-35]. This original research is divided into two major parts: synthesis and PDT application:

(1) To synthesize the nano-based natural Chinese medicine, "curcumin" (Cur-Gd-AuNP), as a PS for PDT (obtained the preliminary results);

(2) Describe and suggest the possible PDT application on Cur-Gd-AuNP for treating Alzheimer's disease (AD) in future development based on the literature review.

## 2. Materials and Methods

To synthesize the Curcumin Gd-AuNP (Cur-Gd-AuNP), it consisted of two steps, including preparation of the backbone Gd-AuNP and polymer capping for encapsulating the Cur-Gd-AuNP [11]:

### *2.1. Gd-AuNP.*

10 nm AuNP was produced by Cline Scientific AB company and used as seeds. AuNP solution was heated to 80°C and stirred vigorously. 200 µl Gd solution (5% w/v) was added and allowed to react for 1 hr. 200 µl Gd solution and 200 µl Sodium Citrate solution were added for another 1 hr. The temperature was increased to 95°C, and 200 µl of Gd solution was added again. The heating was terminated after 45 min, but stirring continued until cooling down. Dialysis was performed overnight.

### *2.2. Curcumin PVP-co-methacrylate Gd-AuNP (Cur-PVP-Gd-AuNP).*

Polymer capping was performed at 80°C during vigorous stirring. 8.5 mg polymer/100 ml AuGdNP solution was added. The solution was heated and stirred continuously for 45 min, then cooled down during stirring. Conjugation of curcumin commenced when the solution was heated to 60°C. 37.5 mg Curcumin was dissolved in 3.75 ml ethanol and added to the heated solution. The heating was terminated 3 hrs later and cooled with stirring. A superfluous amount of curcumin was removed using centrifugation.

**PVP-co-methacrylate was the FDA-approved polymer used to encapsulate the Cur-Gd-AuNP [12]. Its functions were to improve the bioavailability by attaching or entrapping the phytomedicine (e.g., curcumin) and control the rate of Cur-Gd-AuNP release to the target [13].

## 3. Results and Discussion

The Gd-AuNP and Cur-PVP-Gd-AuNP were characterized by (a) Ultra-Violet (UV) and (b) Transmission electron microscope (TEM), respectively.

(a) Ultra-Violet (UV) for the detection of absorption spectrums in Gd-AuNP and Cur-PVP-Gd-AuNP (Figure. 1). AuNP and curcumin were used as references.

In Figure 1, curcumin (green line) and AuNP (blue line) with an absorption peak at 430 nm and 530 nm. The absorption peak of Gd-AuNP (red line) was nearly unchanged at 428-430 nm as it consisted of AuNP only. However, Cur-PVP-Gd-AuNP (purple line) contained two absorption peaks, including 430 nm curcumin and 530 nm AuNP.

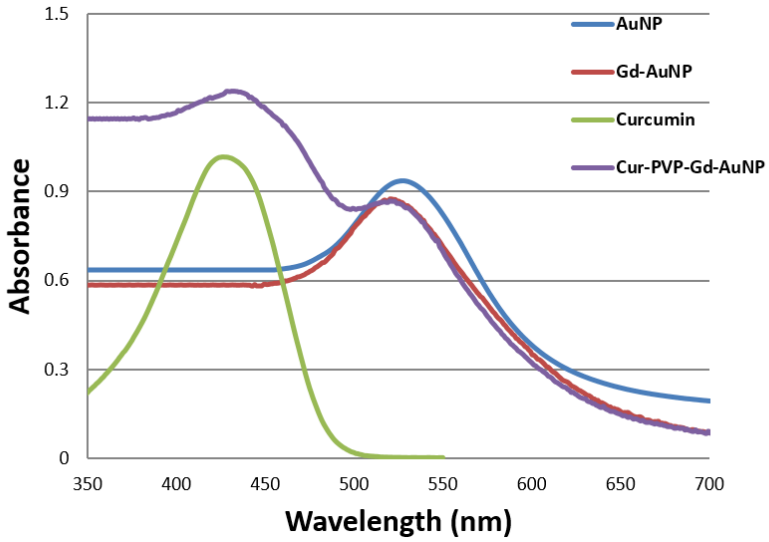


**Figure 1**. UV spectrum of Gd-AuNP and Cur-PVP-Gd-AuNP.

(b) Transmission electron microscope (TEM) was used to determine the morphology and size of Gd-AuNP and Cur-PVP-Gd-AuNP. Based on Figure 2 (Gd-AuNP) and Figure 3 (Cur-PVP-Gd-AuNP), these nanoparticles' morphology was mainly spherical and a goose egg in shape (x 200). Its nanoparticles size was 16.30 ± 6.20 nm and 17.40 ± 5.80 nm for the Gd-AuNP (Figure 4) and Cur-PVP-Gd-AuNP (Figure 5). The diameter of Cur-PVP-Gd-AuNP has become bigger after being linked with the Gd-AuNP.

**Scale bar: 200 nm**

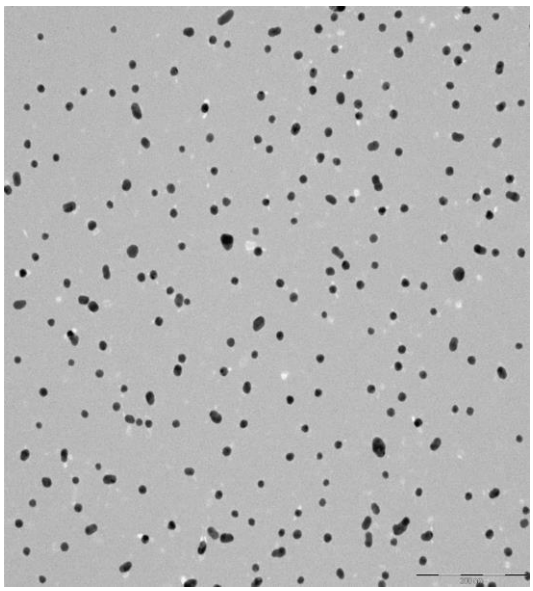

**Figure 2**. Gd-AuNP morphology.

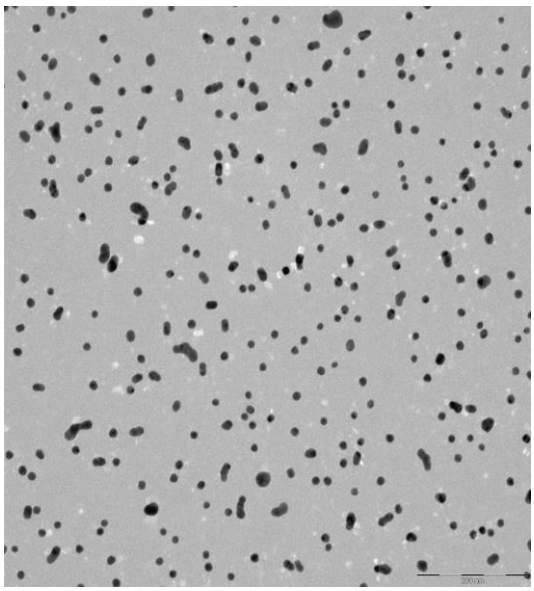

**Figure 3**. Cur-PVP-Gd-AuNP morphology.

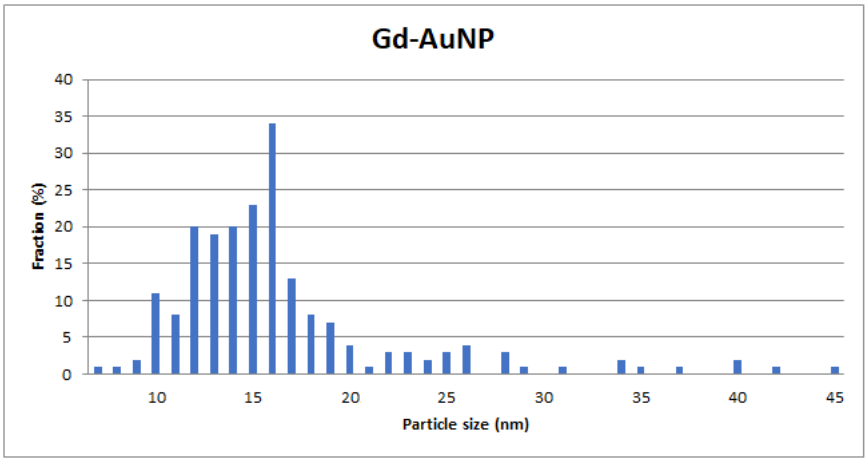


**Figure 4**. Size distribution of Gd-AuNP.

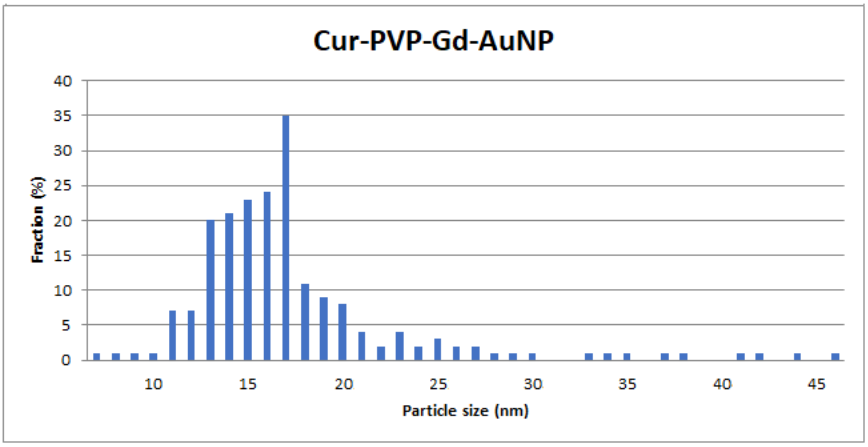


**Figure 5**. Size distribution of Cur-PVP-Gd-AuNP.

By confirming the Ultra-Violet (UV) and (b) Transmission electron microscope (TEM) results, the structure of Cur-PVP-Gd-AuNP was successfully proposed (Figure 6).

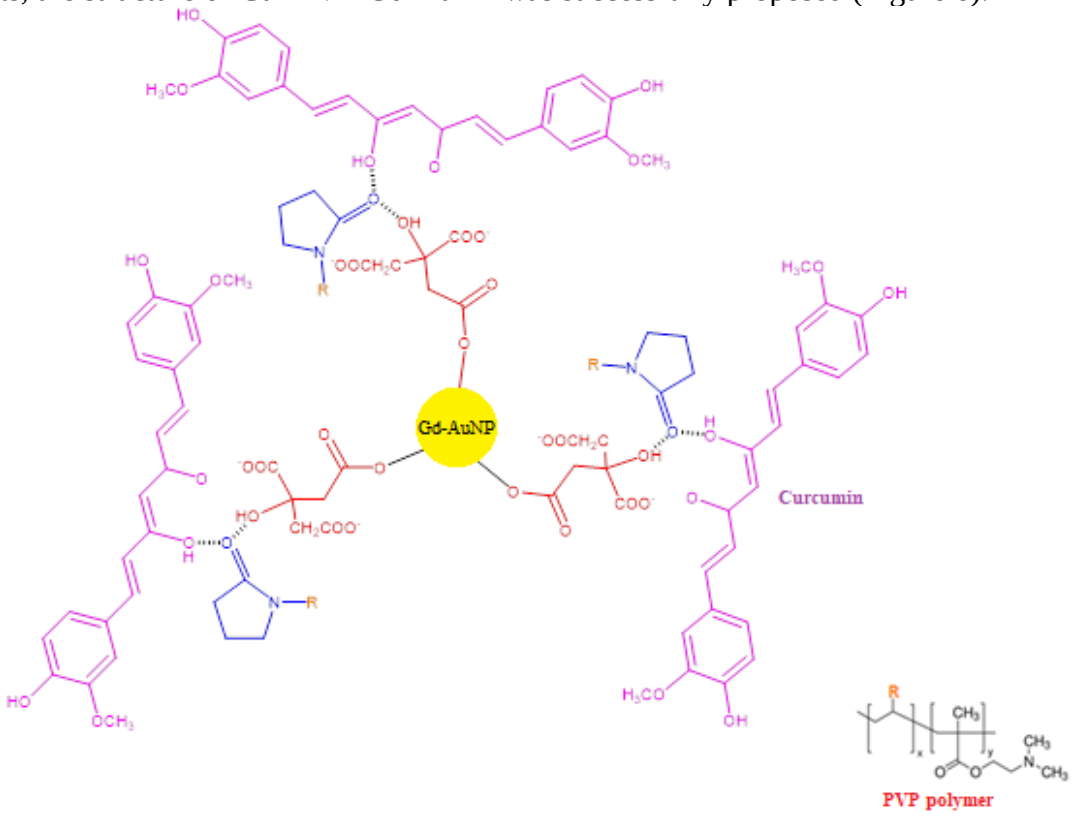


**Figure 6**. Chemical structure of Cur-PVP-Gd-AuNP.

## 4. Conclusions

The expected Cur-PVP-Gd-AuNP structure was synthesized, it will propose the application of PDT to treat AD. Curcumin is a natural PS and has anti-inflammatory properties, which reduces beta-amyloid plaques in the brain. This Cur-PVP-Gd-AuNP may activate within a broad wavelength from 300 to 700 nm with a light dosage of 50 J $cm^{-2}$ generating the ROS to cause cell damage and death through the PDT processes [14]. The bioavailability of curcumin is enhanced by nanotechnology. Although it is non-toxic, much more work needs to be done, such as cytotoxicity and dosage safety assessment in the human study.

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## Conflicts of Interest

The authors declare no conflict of interest.

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