



ORIGINAL ARTICLE

Two Cu(II)-based coordination polymers: Photocatalytic dye degradation and treatment activity combined with BDNF modified bone marrow mesenchymal stem cells on craniocerebral trauma via increasing complement C3 expression

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Abstract Two novel mixed-ligand Cu(II) coordination polymers (CPs) $\{[\text{Cu}_2(\text{edpc})_2(\text{ga})_2]\cdot 2\text{H}_2\text{O}\}_n$ (**1**) and $\{[\text{Cu}(\text{edpc})(\text{bpdc})]\cdot 0.25(\text{H}_2\text{O})\}_n$ (**2**) (H_2ga = glutaric acid, edpc = 9-ethyl-2,6-di-pyridin-4-yl-*H*-carbazole, H_2bpdc = biphenyl-4,4'-dicarboxylic acid) have been solvothermally formed through a π -conjugated carbazole-containing pyridine ligand under the presence of auxiliary ligands (H_2ga for the complex **1** and H_2bpdc for complex **2**). Due to its good water stability of complex **2**, it was applied in the photocatalytic rhodamine B (RhB), methylene blue (MB) and methyl orange (MO) degradation in unclean water, and the possible pathway of photocatalytic degradation was researched. Whether the compounds could enhance the treatment activity of the BDNF modified bone marrow mesenchymal stem cells (BMSC) against craniocerebral trauma was then evaluated. The recognition of the craniocerebral trauma mice was assessed by Morris water maze (MWM). The viability of the nerve cells in the brain was evaluated by Cell Counting Kit-8 (CCK-8). Then the enzyme-linked immuno sorbent assay (ELISA) detection was performed to detect the release

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content of the brain-originated neurotrophic factor and nerve promoting factor β in peripheral regions of cerebral hemorrhage. Finally, the expression levels of the complement C3 receptor on the nerve cells in the brain was also determined.

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1. Introduction

Cranio-cerebral trauma is a disease with a high lethality and disability, which brings a lot of burden to individual humans, families and even the whole society (Previgliano and Soto, 2019). For the treatment of cranio-cerebral trauma, people have been committed to the research about the removal of damaged brain tissue in order to reduce the primary and secondary injuries (Kulkarni et al., 2020). The usage of stem cells for the central nervous system injury treatment is a new strategy for the neural injury therapy that is widely concerned in the academic community at present, which brings a new dawn to the neurorepair treatment after cranio-cerebral injury (Erlangsen et al., 2020). Bone marrow mesenchymal stem cells (BMSC) can be broken up into neuronal cells in vivo, and secrete nerve promoting factors, brain-derived nerve promoting factors, etc. at the same time, and play a protective role in injured nerve tissue (Carballo-Cuello et al., 2020). Thus, in this present research, we aimed to explore the new candidates for the treatment of cranio-cerebral injury, and reveal the related mechanism at the same time.

In recent ten years, new functional coordination polymers (CPs) have attracted more and more attention in gas collection, catalysis, sensing field, magnetic pole, ion exchange and other industries (Lu et al., 2019; Li et al., 2016; Gu et al., 2019a, 2019b; Feng et al., 2019, 2017b). The final reactants are affected by various factors, such as the types of metal ions and organic ligands, synthesis operations, operating temperature, solvent types, molar ratio and pH value (Feng et al., 2017a, 2013; Duan et al., 2020a, 2020b). In a word, a reasonable coordination of organic ligands plays an important role in the structure of target CPs. Based on pyridine derivatives, we have obtained a variety of CPs structures. Among them, *N*-substituted pyridine ligands with rigid spacer group, because of their high thermal stability, effectively decline the unexpected situation of the synthesis. The ligands containing carbazole have strong rigidity, good conjugation, high fluorescence intensity, high catalytic activity and good biological activity, so they are attracting more and more attention (Cheng et al., 2015, 2017; Yi et al., 2014, 2013). So the ligands containing carbazole are regarded as an important component for the formation of CPs. At the same time, organic polycarboxylic acid ligands have been largely used in the construction of metal CPs due to their unique coordination method and high coordination capability to metal ions.

In the present study, two new structure Cu(II) coordination polymers (CPs) $\{[Cu_2(edpc)_2(ga)_2] \cdot n(H_2O)\}_n$ (**1**) and $\{[Cu(edpc)(bpdc)] \cdot 0.25(H_2O)\}_n$ (**2**) (H_2ga = glutaric acid, $edpc$ = 9-ethyl-2,6-di-pyridin-4-yl-9*H*-carbazole, $bpdc$ = biphenyl-4,4'-dicarboxylic acid) have been formed. The novel carbazole-containing pyridine ligand under the circumstance of auxiliary ligands (H_2ga for the complex **1** and H_2bpdc for complex **2**). Due to its good water stability of complex **2**, it was applied to the photocatalytic rhodamine B (RhB), methylene blue (MB) and methyl orange (MO) degradation in unclean water, and the principle of photocatalytic degradation was researched. In biological experiment, the promotion activity of the compound on the brain derived neurotrophic factor (BDNF) modified bone marrow mesenchymal stem cells (BMSC) against cranio-cerebral trauma was assessed in vivo. The results of the Morris water maze (MWM) assay suggested that compound **1** has more powerful promotion ability than compound **2** on the increasing the BMSC treatment effect. The CCK-8 assay suggested that compound **1** could significantly increase the nerve cells viability. The ELISA detection further revealed that the release content of the brain-originated neurotrophic factor and nerve

promoting factor β in peripheral regions of cerebral hemorrhage was obviously increased under compound **1** treatment instead of compound **2**. In the end, the western blot indicated, the enhancement activity of compound **1** was due to the up-regulated expression of the complement C3 receptor on the nerve cells in the brain.

2. Experimental

2.1. Chemicals and measurements

All materials in the experiment were purchased from the Beijing Bailingwei Reagent Company and used in the experiment with no purification. Elemental analysis of carbon, hydrogen and nitrogen was carried out by the PerkinElmer 240C analyzer. The Bruker FTIR spectrometer was used to analyze the samples obtained in the experiment, and the infrared spectrum in the range of $4000\text{--}400\text{ cm}^{-1}$ was recorded. The Lambda 950 UV-vis spectrometer was used to analyze the diffuse reflection spectroscopy (DRS) of the samples in the wavelength range of 200–800 nm. The photocatalysis experiment was carried out using Bilon BL-GHX-V photochemical reactor. The processed materials were evaluated by the JASCO V-550 UV-vis recording spectrophotometry.

2.2. Preparation and characterization for $\{[Cu_2(edpc)_2(ga)_2] \cdot 2H_2O\}_n$ (**1**) and $\{[Cu(edpc)(bpdc)] \cdot 0.25(H_2O)\}_n$ (**2**)

For the synthesis of complex **1**, 12 mg $Cu(NO_3)_2 \cdot 6H_2O$ (0.05 mmol), 6.6 mg H_2ga (0.1 mmol), 8.7 mg $edpc$ (0.05 mmol) and 5 mL of DMF/ H_2O (ratio is 4:1) were mixed to form a solution. Next, the solution was poured into a 25.0 mL Parr Teflon-lined stainless steel vessel, then kept at 115 °C for 72 h. After cooling it to atmospheric temperature, wash the obtained blue shaped crystals and keep them dry. The final result was 45% percent, based on the weight of Cu. Anal. calcd for $C_{58}H_{54}N_6O_{10}Cu_2$: the carbon content is 61.82; the hydrogen content is 4.80; and the nitrogen content is 7.46 percent. Found (experimental): the carbon content is 61.85, the hydrogen content is 4.76 and the nitrogen content is 7.49 percent. IR (KBr, cm^{-1}): 3401(vs), 1607(vs), 1479(s), 1388(vs), 1294(m), 1228(s), 1162(s), 1133(w), 1071(w), 1036(w), 886(w), 807(s), 751(m), 682(w), 641(w), 608(w), 526(m).

For the synthesis of complex **2**, 12 mg $Cu(NO_3)_2 \cdot 6H_2O$ (0.05 mmol), 12.1 mg H_2bpdc (0.05 mmol), 8.7 mg $edpc$ (0.05 mmol) and 5 mL of DMF/ H_2O (ratio is 4:1) were mixed to form a solution. Next, the solution was poured into a 15 mL Parr Teflon-lined stainless steel vessel, then kept at 100 °C for 72 h. After cooling it to atmospheric temperature, wash the obtained blue shaped crystals and keep them dry. The final result was 45% percent, based on the weight of Cu. Anal. calcd for $C_{38}H_{27.5}N_3O_{4.25}Cu$: the carbon content is 69.14; the hydrogen content is 4.10; and the nitrogen content is 6.37 percent. Found (experimental): the carbon content is 68.74, the

hydrogen content is 4.23 and the nitrogen content is 6.26 percent. IR (KBr, cm^{-1}): 3409(s), 1678(s), 1610(vs), 1544(m), 1479(vs), 1381(vs), 1294(s), 1222(s), 1131(w), 1090(w), 1037(m), 1011(s), 844(s), 808(s), 773(vs), 686(s), 606(m), 529(w), 438(m).

In order to obtain the data of X-ray, we use the Oxford Xcalibur E diffractometer. Statistical analysis of various strength data was performed using crystalispro software and the results were converted to HKL format. The pattern of SHELXS based on direct means was applied for establishing the initial structure models, and the pattern of SHELXL-2014 based on least square method was altered. The atom except hydrogen atom is refined by using different heterogeneous parameters. Next, the whole of H atoms by using AFIX program to fasten on the C atom they are connected to. Table 1 shows the parameters and details of complex **1** and **2**.

2.3. Photocatalytic activity test

The photocatalytic activities of complexes **1** and **2** were evaluated by the photodegradation of RhB, MB and MO solutions at ambient temperature (298 K). The photocatalytic reactions were performed by a typical process: 25 mg of the coordination complex was dispersed in 100 mL aqueous solution of MB (6 mg L^{-1}), MO (6 mg L^{-1}) or RhB (6 mg L^{-1}) under a UV lamp, respectively. Before turning on the Hg lamp (400 W), the mixture was magnetically stirred in the dark for 30 min until an adsorption-desorption equilibrium was established

at given intervals, and 5 mL of the reaction solution was periodically taken from the reactor and dispersed powders were removed by centrifugation. The separated samples were analyzed by UV-vis spectrophotometry. Degradation of the organic dyes under UV light irradiation without any complexes was also carried out for comparison.

2.4. Morris water maze (MWM)

After the synthesis of compounds **1** and **2** in this present research, their enhancement activity against craniocerebral trauma after planted with BDNF mesencephalic mesencephalic stem cells were evaluated by determining the cognitive function in mice. Thus, the Morris water maze measurement was operated in the study under the instructions. In short, the 50 mice used in the study were obtained from the Zhejiang university (Hangzhou, China) and then kept at the standard environment with ample water and aliment. All the operation in the study was adopted by the Ethics Committee of the Zhejiang university (Hangzhou, China). Intracerebral hemorrhage model was made by injecting heparin and collagen using brain stereotactic method. Three days later, GDNF/BMSCs were transplanted into brain combined with compound **1** or **2** for treatment at the concentration of 5 mg/kg for 12 h. The MWM was conducted and the time of the mice finished the MWM was recorded and analyzed.

2.5. Cell Counting Kit-8 (CCK-8)

To evaluate the viability of the nerve cells in the brain during craniocerebral trauma, the Cell Counting Kit-8 was operated in the study after compound **1** or **2** treatment with GDNF/BMSCs transplantation. All the preformation was finished according to the protocols. In short, the growing neurons in the logical growth were collected and seeded into 96 well plates at the concentration of 10^4 cells per well. The neurons were first cultured at 37°C and $5\% \text{ CO}_2$ for 12 h, then incubated with compounds **1** and **2** (1, 2, 4, 8, 10, 20, 40, 80 $\mu\text{g/mL}$) for 48 h. Next, the cell medium was removed and replaced with new medium with 10% CCK-8 reagent. Finally, the absorbance of each wells was measured and analyzed from three repeats.

2.6. ELISA detection

After compound **1** or **2** treatment, the content of the brain-originated neurotrophic factor and nerve promoting factor β released into peripheral regions of cerebral hemorrhage was evaluated by ELISA detection kit. This measurement was conducted in accordance with the instruments with a little modification. Briefly, the brain stereotactic method was used to establish the hemorrhage model, then the GDNF/BMSCs were transplanted into brain combined with compound **1** or **2** for treatment at the concentration of 5 mg/kg for 12 h. Subsequently, the cerebrospinal fluid of the mice in different groups was collected and the quantity of growth factors was evaluated. This study was conducted three times and the results were showed as mean \pm SD.

Table 1 Refinement details and crystallographic parameters for complexes **1** and **2**.

Identification code	1	
Empirical formula	$\text{C}_{58}\text{H}_{54}\text{Cu}_2\text{N}_6\text{O}_{10}$	
Formula weight	1122.15	652.07
Temperature/K	296.15	293(2)
Crystal system	monoclinic	monoclinic
Space group	$\text{P}2_1/\text{c}$	$\text{C}2/\text{c}$
a/ \AA	18.720(2)	5.2980(11)
b/ \AA	14.3740(10)	5.58(2)
c/ \AA	10.0132(6)	8.1865(6)
$\alpha/^\circ$	90	90
$\beta/^\circ$	109.0(3)	98.9290(10)
$\gamma/^\circ$	90	90
Volume/ \AA^3	5268.0(10)	3460.2(4)
Z	4	4
$\rho_{\text{calc}}/\text{g cm}^{-3}$	1.15	1.252
μ/mm^{-1}	0.673	0.673
Data/restraints/parameters	9185/0/675	3049/70/215
Goodness-of-fit on F^2	1.014	1.088
Final R indexes [$I \geq 2\sigma(I)$]	$R_1 = 0.0403$, $\omega R_2 = 0.1112$	$R_1 = 0.0673$, $\omega R_2 = 0.1947$
Final R indexes [all data]	$R_1 = 0.0493$, $\omega R_2 = 0.1151$	$R_1 = 0.0768$, $\omega R_2 = 0.2024$
Largest diff. peak/hole/ $e \text{ \AA}^{-3}$	0.77/−0.85	0.70/−0.61
CCDC	1,999,757	1,999,768

2.7. Western blot

The western blot was carried out to evaluate the expression ability of the complement C3 receptor on the nerve cells differentiated from GDNF/BMSCs in the brain. All preformation was under the manufactures' protocols. Briefly, the brain stereotactic method was used to establish the hemorrhage model, then the GDNF/BMSCs were transplanted into brain combined with compound 1 or 2 for treatment at the concentration of 5 mg/kg for 12 h. The nerve cells in the brain were collected and the total protein was extracted. The BCA detection kit was used to evaluate the protein concentration. Next, all the samples were loaded on SDS-PAGE gel and electrophoretically transferred to a 0.22 mm (PVDF) membrane. After blocked with 5% nonfat milk for 2 h, the primary antibody and secondary antibody conjugated with horseradish peroxidase was used to incubate the PVDF membrane. Chemi-Doc™ Touch Imaging System (Bio-Rad, Hercules, California, USA) was used to capture the images.

3. Results and discussion

3.1. Molecular structure

According to the results of single crystal X-ray diffraction, complex **1** crystallized in monoclinic $P2_1/c$ space group. The asymmetric part of **1** is composed of two mutually independent

Cu(II) cations, double edge ligands and two different ga^{2-} anions. Fig. 1a shows that the coordination structures of Cu(1) and Cu(2) are different. Cu(1) atom is composed of two O atoms from different ga^{2-} and two N atoms from different edge ligands to form a five coordinated form, which is a twisted triangular biconical structure $[CuN_2O_3]$. Cu(2) atom is surrounded by four O atoms of two kinds of ga^{2-} and two N atoms from different edge ligands. It has a deformed $[CuN_2O_4]$ octahedral geometry. The length of Cu-N bond is 1.980(2) to 2.074(2) Å and the length of Cu-O bond is 1.902(2) to 1.953(3) Å, all of which are normal. There are two different coordination modes of ga^{2-} anions in **1**. Fig. 1b shows that deproton carboxyl group of the H_2ga ligand coordinates with Cu(1) is in the mode of $\mu_1-\eta^1:\eta^1$, and the H_2ga ligand coordinated with Cu(2) is in the mode of $\mu_1-\eta^1:\eta^1$ and $\mu_2-\eta^1:\eta^0$. As shown in Fig. 1c, the edge ligand bridges the two Cu(II) cations to the left-handed helical chain L1 along the b -axis by two of its arms in the form of μ_2 bridging coordination, while the carboxyl group from ga^{2-} bridges the two Cu(II) cations to the left-handed helical chain L2 along the c -axis according to Fig. 1d, the adjacent helical chains form a two-dimensional structure based on the same Cu(II) cations interconnection. Through topological analysis, this structure can be clearly shown. Taking Cu(II) as a 4-connection node, ga^{2-} and edge anion as junctions, **1** can be seen as a 4-connection sql network with the dot symbol $\{4,6\}$. The lattice water molecule O10 forms a strong hydrogen bond between the (4,4) network layer and the coordination carboxylic oxygen atoms O4, O5. The Cu(1) cation bridge is

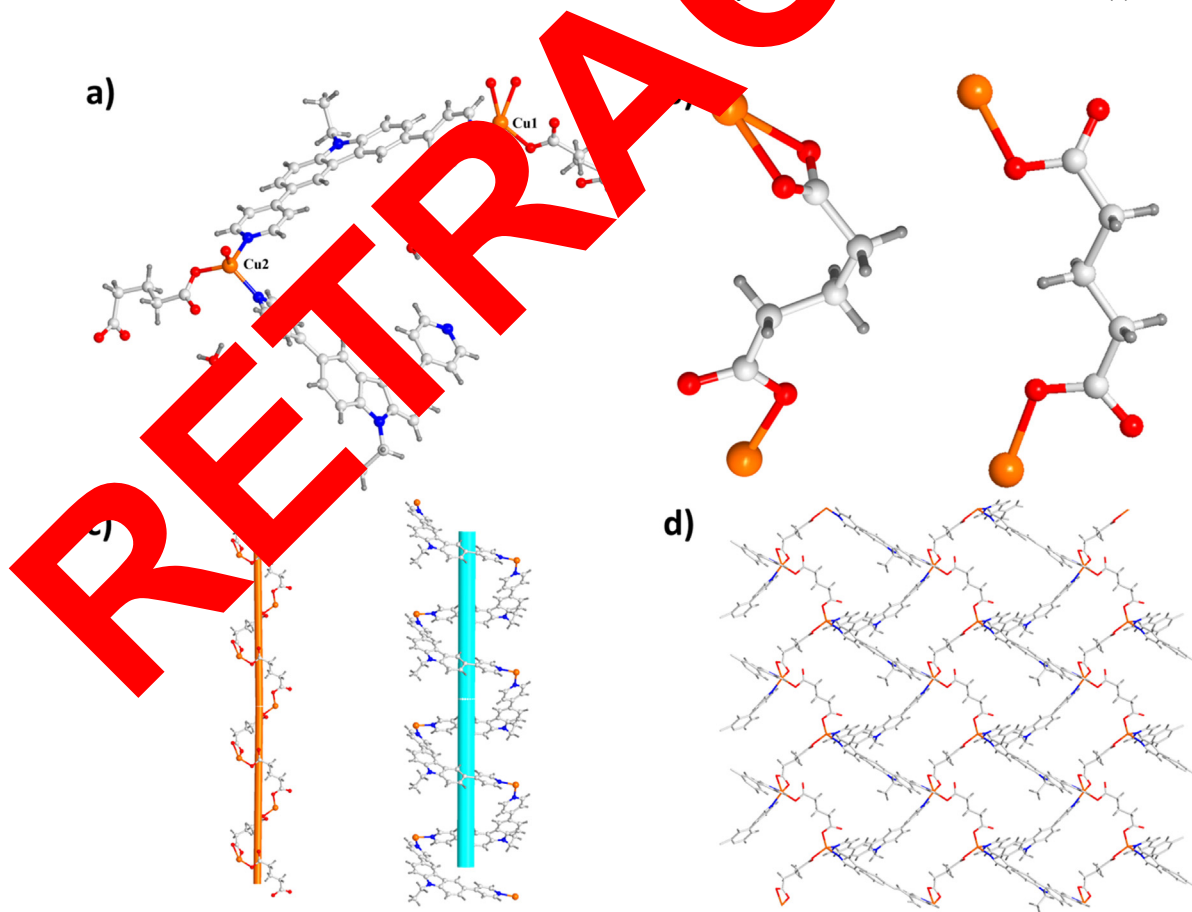


Fig. 1 (a) Image for the asymmetry part of **1**. (b) The coordination modes for the ga^{2-} ligands. (c) The helical chains found by link of the ligands with the Cu(II) ions. (d) The 2D layered framework of **1**.

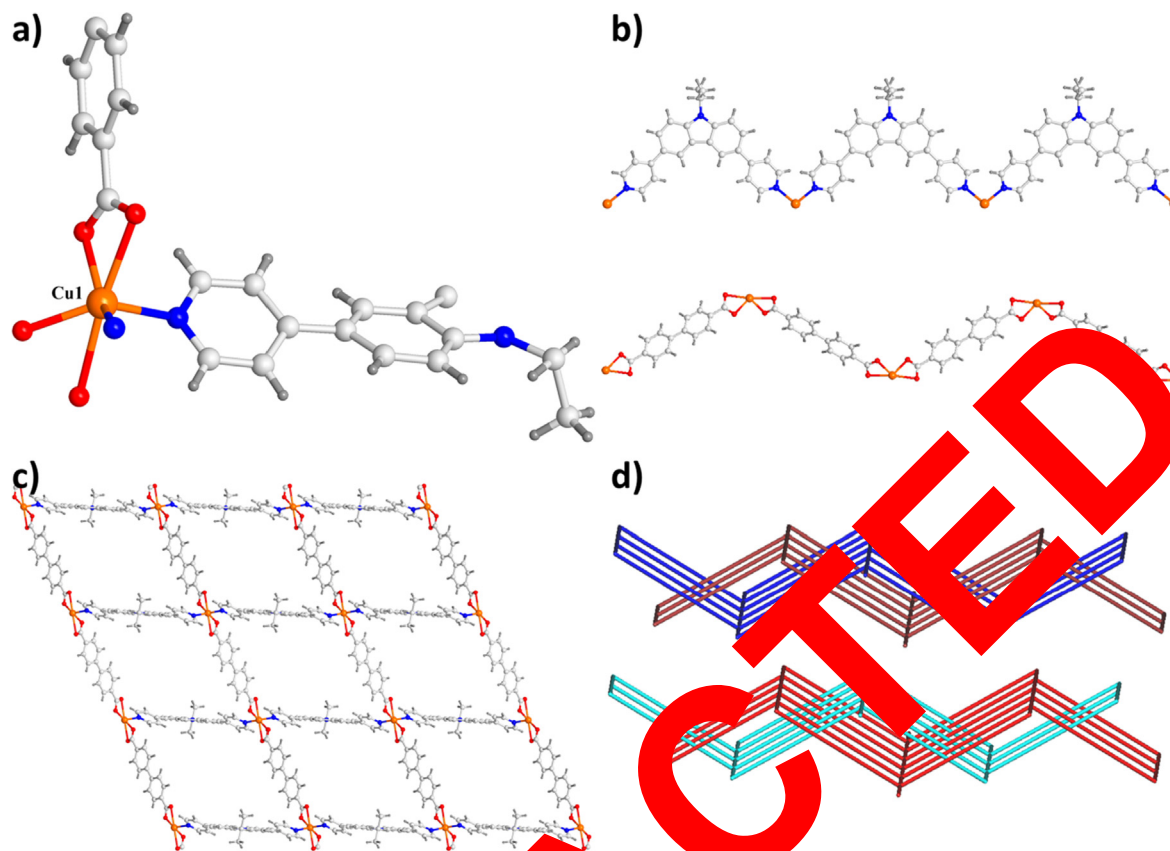


Fig. 2 (a) Image for asymmetric part of complex **2**. The 1-dimensional chains found by the link of the ligands with Cu(II) ions. (c) The two-dimension layered framework of **2**. (d) The 2-fold interpenetrated framework of complex **2**.

connected to the right-hand helical chain R_{\parallel} along the a axis. In addition, the adjacent two-dimensional framework R_{\perp} along the b axis is connected in a $\cdots A A A A \cdots$ parallel is connected in a two-dimensional layered structure through the hydrogen bond.

According to the results of single-crystal X-ray diffraction, complex **2** belongs to the monoclinic $C2/c$ space group. The asymmetric part of **2** consists of a single Cu(II) ion, a single edpc ligand, a single bpdca²⁻ ligand and a quarter of water molecule. Fig. 2a shows that Cu(II) is hexacoordinated in octahedral coordination environment, which is formed by four O atoms from two chelated bpdca²⁻ ligands and two N atoms from different edpc ligands. As shown in Fig. 2b, edpc ligands connect Cu(II) cations to shape an infinite one-dimensional linear chain. The distance between two adjacent Cu(II) ions is 2980 Å, and the angle of Cu-Cu-Cu is 180°. Next, through the coordination of the carboxyl group of bpdca²⁻ with Cu(II) cation, another infinite one-dimensional zigzag chain with Cu-Cu distance of 15.1678 Å and Cu-Cu-Cu angle of 124.475° is formed. In the end, the two chains are connected in a highly undulating two-dimension framework. In this structure, every 6-membered ring is shaped by 4 Cu(II) cations, 2 edpc and 2 bpdca²⁻ ligands, with a size of 25.2943 × 16.9816 Å (diagonal length). From the topological point of view, Cu(II) cation can be regarded as 4-connected nodes, and edpc and bpdca²⁻ ligands can be regarded as connectors; therefore, two-dimension network can be written as a stacked 4⁴-6²-sql framework, including a window of 15.298 × 14.805 Å (Fig. 2c). The high fluctuation of such a

large network window and a sql table admits two adjacent tables to infiltrate each other in a parallel pattern, thus forming a 2D framework (Fig. 2d).

3.2. Photocatalytic activities

Fig. 3 shows the UV/Vis reflection spectra of **1** and **2**. According to the graph drawn by Kubelka-Munk method $(F(R)/hm)^{0.5}$, band gap energy E_g was defined by the intersection of the energy axis and the line extrapolated from the linear part of the absorption edge, where h represents the Planck constant, M represents the frequency of electromagnetic wave, and R represents the reflectivity of infinite thick layer at a certain wavelength. As for the Kubelka-Munk method, $F(R) = (1 - R)^2/2R$ was transformed from the logged diffuse reflection data. As shown in Fig. 3, the E_g estimate of **1** is 3.28 eV, and that of **2** is 2.71 eV. It is suggested that complexes **1** and **2** may respond to UV light and have potential photocatalytic activity. Considering the following dye degradation experiments, it is essential to research their water stability. Complexes **1** and **2** were soaked in water and the results show that complex **1** quickly decomposes while complex **2** could keep its crystallinity.

The catalytic properties of complex **2** were studied by measuring the effects of complex **2** on rhodamine B (RhB), methylene blue (MB) and methyl orange (MO), which are common organic dyes in the industrial wastewater (Banasz and Wałęsa-Chorab, 2019; Yuan et al., 2020; Ren et al., 2017;

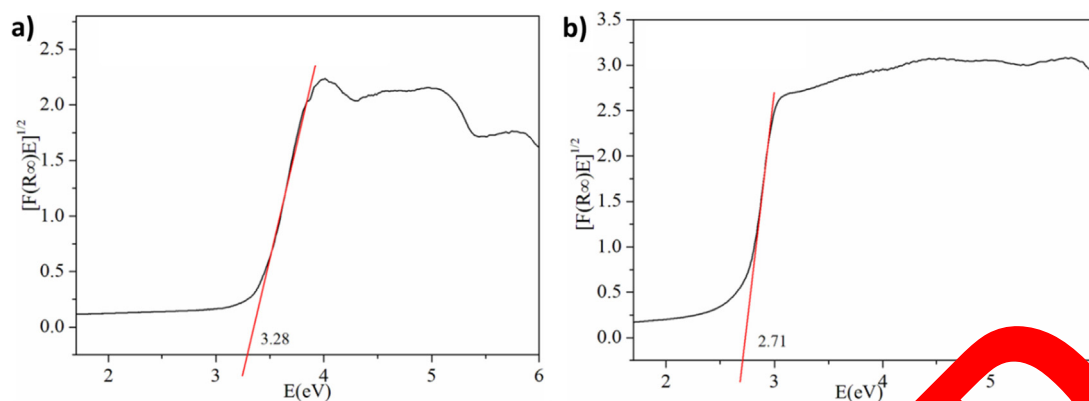


Fig. 3 the UV/V reflection spectra and energy (eV) of 1 (a) and 2 (b).

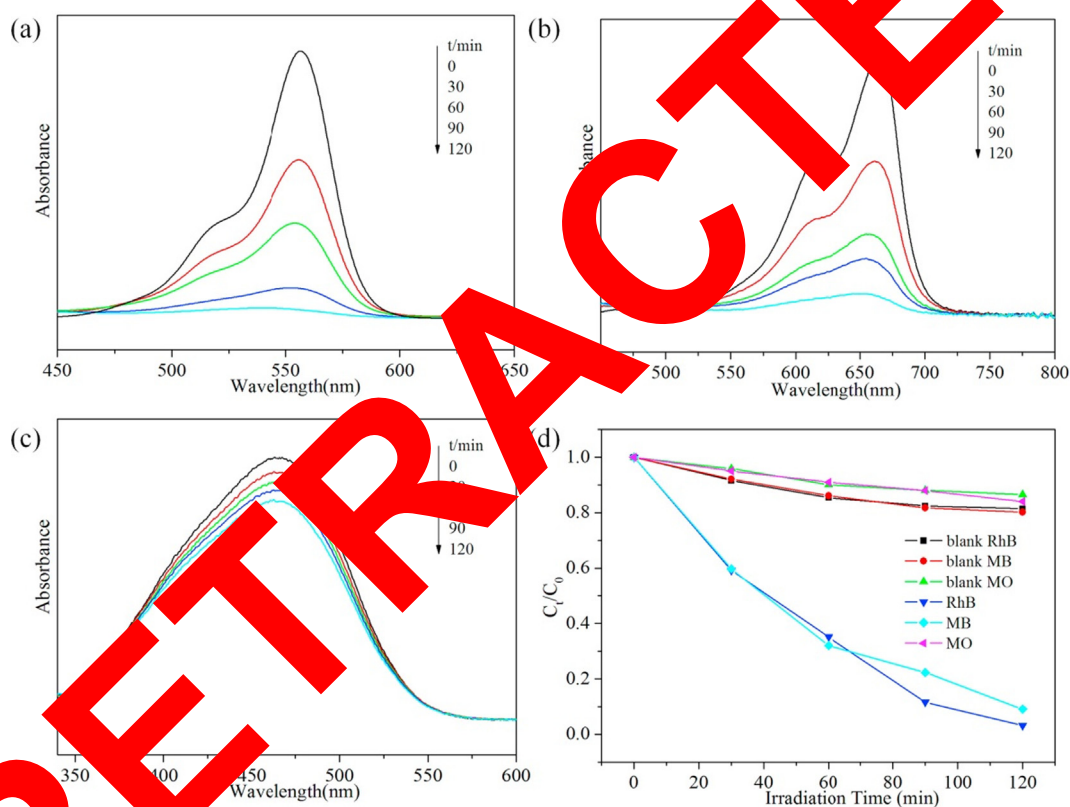


Fig. 4 Absorption spectra of (a) RhB, (b) MB and (c) MO solution during the degradation reaction by using 2; (d) plots of concentration ratios of RhB, MB and MO C_t/C_0 against irradiation time (min) under the circumstance of 2 during the degradation reaction under UV irradiation.

Patroniak et al., 2006; Marcinkowski et al., 2017, 2015; Wei et al., 2020; Jawad et al., 2019, 2016, 2015; Jawad, 2019). It should be noted that as a kind of photocatalyst, 2 is insoluble in water. Therefore, the experimental conditions were 165 W mercury lamp ultraviolet light irradiation, and the photocatalytic activity of 2 was assessed by reacting with these dye solutions. We monitored the decomposition of RhB, MB and MO at 464 nm, 544 nm and 664 nm. At the same time, we gave the time-resolved absorption spectra of 2 for three substances.

Fig. 4a shows the degradation of RhB solution by 2. According to the figure, the maximum absorbance of the solution at 554 nm decreased gradually with the increase of illumination time. Moreover, the decomposition rate of RhB was 97% after two hours of UV irradiation and half an hour of standing. Fig. 4b shows the degradation of MB by 2. The decomposition rate of MB was 91% after two hours of UV irradiation. In the same environment, the photocatalytic degradation of MO by complex 2 is weak (Fig. 4c). Fig. 4d shows that under UV irra-

diation, the decomposition rate of MB, RhB and Mo at the circumstance or absence of **2**. So the complex is very good at photocatalytic degradation of RhB and MB. To detect this selective effect, we compared the structures of MB, MO and RhB. It could be found that MO has azo groups, but RhB and MB have different structures. For complex **2**, the selective degradation of RhB and MB may depend on whether the structure of the pollutant contains azo group.

Based on the literature review and the above experiments, the following conclusions about the photocatalytic mechanism of degradation are obtained (Jawad et al., 2019, 2016, 2015; Jawad, 2019). In the UV environment, the electrons (e^-) in the highest polymer orbit are excited and transferred to the lowest unoccupied molecular orbit, leaving holes (h^+) in Homo. The e^- and h^+ transfer to the surface of catalyst, and oxygen molecules (O_2) are transformed to oxygen radicals ($\cdot O_2^-$) by electrons, and finally converted to hydroxyl radicals ($\cdot OH$). At the same time, h^+ oxidize H_2O to hydroxyl radicals ($\cdot OH$). These $\cdot OH$ have the ability to disintegrate organic dyes efficiently.

3.3. Compound shortened the time spent by the mice in finishing MWM assay

Compounds **1** and **2** were synthesized for the evaluation of the enhanced activity against craniocerebral trauma after treatment with GDNF/BMSCs. Thus, the MWM assay was performed in this experiment to detect the time spent by the mice finishing this experiment. Fig. 5 indicates that after transplantation of the GDNF/BMSCs in the mice brain, the time spent by the mice in finishing MWM assay was slightly shortened. On the 7th day, the normal animal spent about 5 min during the finishing MWM assay, while the model mice spent about 17 min, which is significantly higher than the control group. However, in combination with compound **1**, the spent time was obviously reduced to 6 min and 11 min, respectively, which is significantly differs from the GDNF/BMSCs group. While, compound **2** showed almost no enhancement activity on the time shorting.

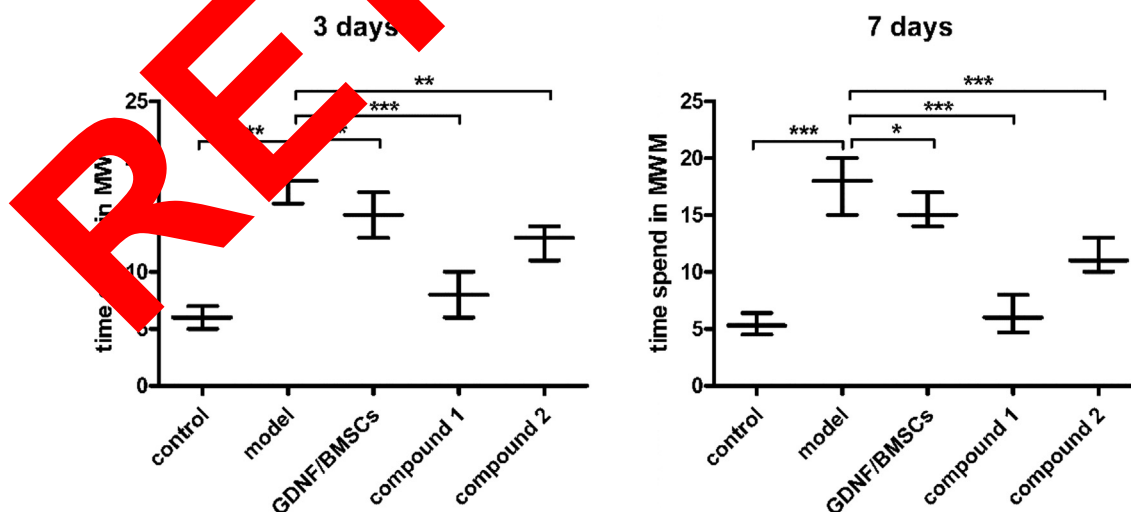


Fig. 5 Shortened time spent by the mice in finishing MWM assay under compound treatment after GDNF/BMSCs transplantation. The brain stereotactic method was used to establish the hemorrhage model, then the GDNF/BMSCs were transplanted into brain combined with compound **1** or **2** for treatment. The MWM assay was conducted to evaluate the cognitive function of the mice.

3.4. Compound increased the viability of the nerve cells

As we have proved in the above results, compound **1** displayed more powerful protective activity on the hemorrhage model than compound **2**. So, in the study, the effect of the compounds on the activity of the nerve cells was also determined. Fig. 6 indicated that the during damaging procession compound **1** treatment could obviously raise the survival rate of the nerve cells, while compound **2** conducted no influence on the cell activity. This result was consistency with the previous results showed in Fig. 6.

3.5. Compound increased the content of brain-derived neurotrophic factor and nerve growth factor β in peripheral regions of cerebral hemorrhage

As the nerve cells differentiated from GDNF/BMSCs in the brain could produce the nerve growth factor β in peripheral regions of cerebral hemorrhage, which is vital important for the nerve cells survival and growth. In this research, the ELISA detection method was used to the concentration measurement of the growth factor in the peripheral regions of cerebral hemorrhage. The data in Fig. 7 indicated that in the model group there was less growth factors than other groups. While, after compound **1** treatment combined with GDNF/BMSCs transplantation, the releasing levels of the growth factors were significantly increased, but the biological function of compound **1** was not observed (see Fig. 8).

Compound stimulated the expression level of the complement C3 receptor on the nerve cells differentiated from GDNF/BMSCs

The complement C3 receptor on the nerve cells could not only regulate the secretion of the brain-original neurotrophic factor and nerve promoting factor β into peripheral regions of cerebral hemorrhage, but also influence the survival and growth of the nerve cells. So the western blot in this this research

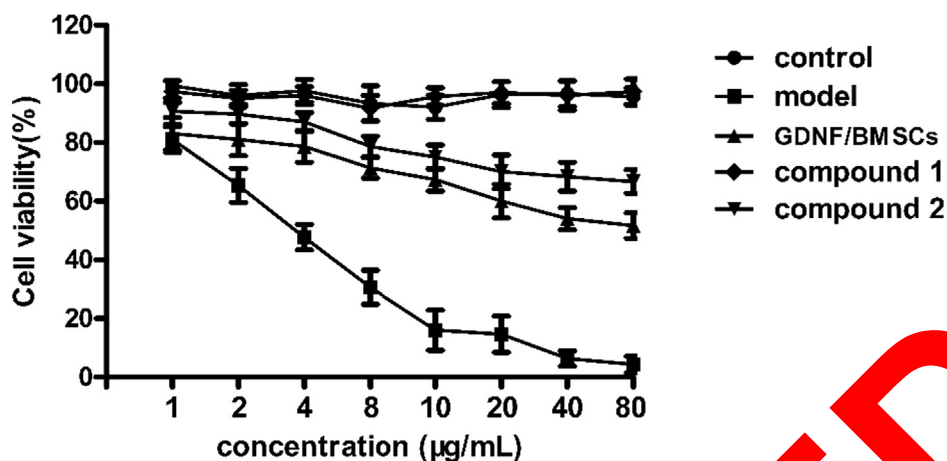


Fig. 6 Increased viability of the nerve cells after compound exposure. The nerve cells were plated into 96 well plate and undergo the hypoxia treatment, then compound 1 or 2 was used for treatment. The CCK-8 was conducted for the live cell assessment.

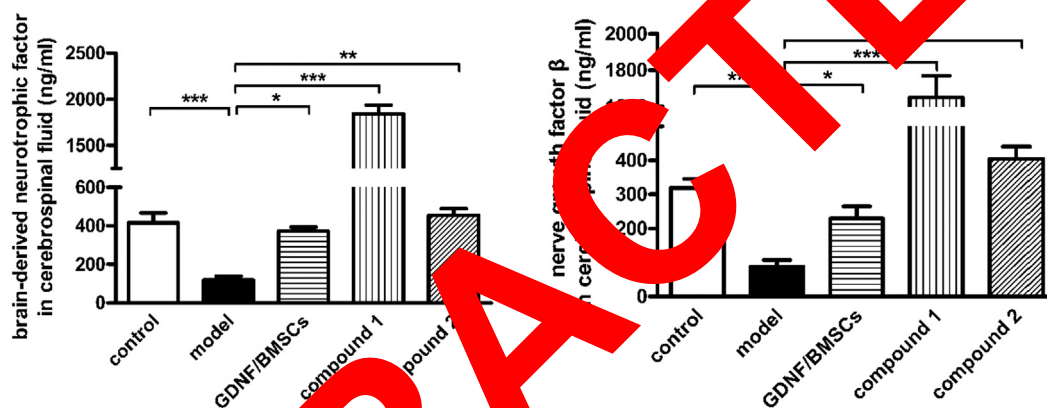


Fig. 7 Increased content of brain-origin neurotrophic factor and nerve promoting factor β in peripheral regions of cerebral hemorrhage. The brain stereotactic method was used to establish the hemorrhage model, then the GDNF/BMSCs were transplanted into brain combined with compound 1 or 2 for treatment. The growth factors in peripheral regions of cerebral hemorrhage were evaluated with ELISA detection kit.

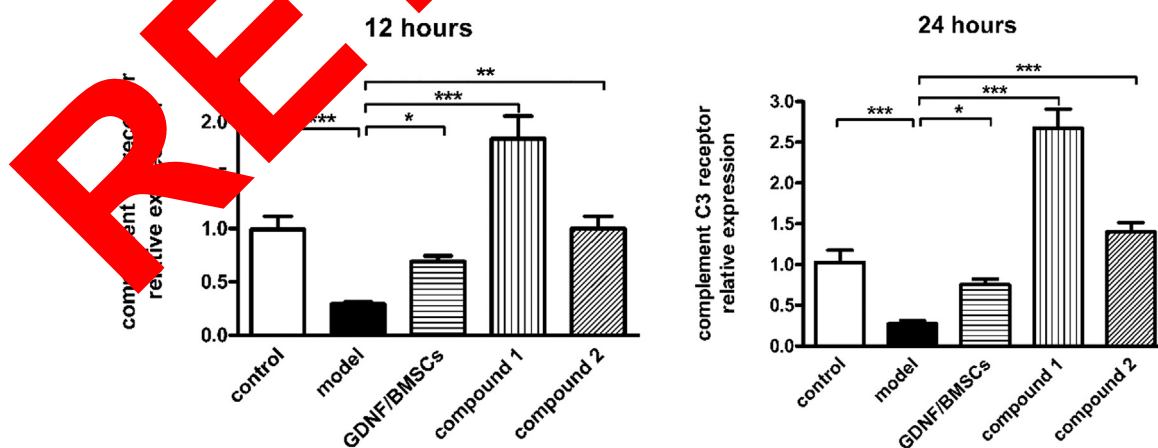


Fig. 8 Stimulated expression level of the complement C3 receptor on the nerve cells differentiated from GDNF/BMSCs under compounds treatment. The brain stereotactic method was used to establish the hemorrhage model, then the GDNF/BMSCs were transplanted into brain combined with compound 1 or 2 for indicated treatment. Western blot conducted in the study was used for complement C3 receptor expression measurement.

was used to determine the complement C3 receptor expression level on the cells. Compared with the model group or the GDNF/BMSCs group, compound **1** could further increasing the up-regulated level of complement C3 receptor on the nerve cells. Total different from compound **1**, compound **2** has no incentive function on the C3 receptor expression.

4. Conclusion

In conclude, we have smoothly formed two fresh mixed Cu(II) coordination polymers (CPs) through a π -conjugated carbazole-containing pyridine ligand under the circumstance of auxiliary ligands (H_2ga for complex **1** and H_2bpdc for complex **2**). The single crystal X-ray diffraction research shows that complex **1** shows a 2D layered framework based on the helical chains and complex **2** demonstrates a 2-fold interpenetrated network. Due to its good water stability of complex **2**, it was applied in the photocatalytic rhodamine B (RhB), methylene blue (MB) and methyl orange (MO) degradation in unclean water, and the principle of photocatalytic degradation was researched. In addition, serious experiments were performed to detect the promotion activity of the compound on the BDNF modified bone marrow mesenchymal stem cells (BMSC) against craniocerebral trauma. We found that compound **1** has more powerful incentive function than compound **2** on the increasing the BMSC treatment effect, which is confirmed by the Morris water maze (MWM) assay. The CCK-8 assay pointed out that compound **1** could significantly increase the nerve cells viability. The ELISA detection further revealed that the release content of the brain-original neurotrophic factor and nerve promoting factor β in peripheral regions of cerebral hemorrhage was obviously increased under compound **1** treatment instead of compound **2**. In the end, the western blot pointed out that the enhancement activity of compound **1** was sue to the up-regulated expression of the complement C3 receptor on the nerve cells in the brain. In conclusion, compare with compound **2**, compound **1** is more talent on the promotion activity of BDNF modified bone marrow mesenchymal stem cells (BMSC) against craniocerebral trauma.

5. Data availability

The data used to support the findings of this study are included within the article.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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