Notice

DESCRIPTION CN102515283A

A method for preparing magnetic iron oxide nanoparticles that can be stably dispersed in water

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一种能稳定分散于水中的磁性氧化铁纳米粒子的制备方法

[0001]

Technical Field

技术领域

[0002]

This invention pertains to the fields of materials chemistry, nanoscience, and biomaterials, and specifically relates to a method for preparing magnetic iron oxide nanoparticles that can be stably dispersed in water.

本发明所属技术领域为材料化学、纳米科学、生物材料领域，特别涉及一 种能稳定分散于水中的磁性氧化铁纳米粒子的制备方法。

[0003]

Background Technology

背景技术

[0004]

γ-Fe₂O₃ with spinel structure or Fe₃O₄ with anti-spinel structure are paramagnetic. According to the grain size, they are further

subdivided into small-particle iron oxide nanoparticles (SPIO: hydrodynamic particle size is approximately 40-180 nm) and ultra-small-particle iron oxide nanoparticles (USPIO: hydrodynamic particle size is less than 40 nm).

尖晶石结构的γ-Fe₂O₃或反尖晶石结构的Fe₃O₄具有顺磁性，按晶粒粒径大 小又细分为小粒子氧化铁纳米粒子(SPIO：水动力学粒径大致在40～180nm) 及超小粒子氧化铁纳米粒子(USPIO：水动力学粒径小于40nm)。

USPIO exhibits superparamagnetism at room temperature, meaning it becomes magnetic when magnetized in an external magnetic field, and its remanence is zero or minimal when the external magnetic field strength is zero.

USPIO在室温 下可表现出超顺磁性，即在外磁场下受磁化而具有磁性，而当外磁场强度为零 时其剩磁为零或极小。

The extremely low remanence of superparamagnetic particles prevents them from agglomerating, allowing them to disperse in solvents.

超顺磁性粒子极低的剩磁使其避免聚集，在溶剂里可以 分散。

Superparamagnetic iron oxide nanocrystals have high magnetic susceptibility and are easily controlled by external magnetic fields. Larger-sized SPIO particles also have their own unique applications.

超顺磁性氧化铁纳米晶粒具有高的磁化率，容易被外磁场控制。 较大粒 径的SPIO也有其特殊的应用。

[0005]

The surface modification of iron oxide nanoparticles directly determines their application fields and effects. Commonly used iron oxide particle modifiers include polymers such as dextran and its derivatives, polyethylene glycol and its derivatives, small molecules such as citric acid and tetramethylamine hydroxide, and inorganic substances such as SiO2, CdS, Au, and Pt.

氧化铁纳米粒子的表面修饰直接决定其应用领域及效果，常用的氧化铁粒 子修饰剂有葡聚糖及其衍生物、聚乙二醇及其衍生物等高分子，柠檬酸、四甲 基氢氧化胺等小分子，SiO₂、CdS、Au、Pt等无机物。

Currently, two types of magnetic iron oxide nanoparticle intravenous injection products, Ferumoxide modified with dextran and Ferucarbotran modified with carboxyl dextran, have been commercialized. Carboxylated polyethylene glycol-modified iron oxide nanoparticles have a longer blood half-life. As a contrast enhancer, the size and surface modifiers of iron oxide nanoparticles determine the probability of them being discovered and phagocytosed by phagocytes in organisms, which in turn determines their distribution specificity or selectivity. Iron oxide nanoparticles have been used in in vivo and in vitro biomedical research, such as magnetic resonance imaging (MRI, fMRI), cell separation and labeling, DNA separation, tumor detection, magnetothermal therapy, and targeted drug delivery (Yang Wensheng, Gao Mingyuan, Bai Yubai). Nanomaterials and biotechnology. Beijing: Chemical Industry Press, 2005.

目前修饰以葡聚糖的 Ferumoxide及修饰以羧基葡聚糖的Ferucarbotran两种磁性氧化铁纳米粒子静脉注射产品已经商品化。 羧基聚乙二醇修饰的氧化铁纳米粒子具有更长的血液 半衰期。 作为造影增强剂，氧化铁纳米粒子的尺寸及表面修饰剂决定了其被生 物体内吞噬细胞发现和吞噬的几率，也就决定了其分布特异性或选择性。 氧化 铁纳米粒子被用于体内(in vivo)和体外(in vitro)生物医学研

究，如磁 共振成像(MRI，fMRI)、细胞分离与标记、DNA分离、肿瘤的检测、磁热治疗 及靶向药物载体等(杨文胜，高明远，白玉白. 纳米材料与生物技术. 北京：化学工业 出版社，2005)。

[0006]

Commonly used methods for preparing iron oxide nanocrystals include coprecipitation, microemulsion, and ultrasonic cavitation.

常用的氧化铁纳米晶粒制备方法有共沉淀法、微乳液法、超声空化法等。

The coprecipitation method involves simultaneously hydrolyzing and precipitating Fe³⁺ and Fe²⁺ salts in an aqueous solution at a molar ratio of 2:1, or partially oxidizing and precipitating Fe²⁺ salt in the presence of an oxidant to achieve the synthesis of Fe₃O₄ nanocrystals. The coprecipitation method has the advantages of being simple and inexpensive. However, the coprecipitation method has the disadvantages of wide particle size distribution and easy agglomeration. Moreover, since the reaction between iron oxide and water is relatively complex and can

generate a variety of compounds, other phase impurities are often mixed into the product, which cannot give full play to the role of nano iron oxide in biological systems. Nano-iron oxide prepared by the improved microemulsion method and ultrasonic cavitation method generally suffers from poor crystallinity, low magnetic properties, and difficulty in controlling particle size and morphology.

共沉淀法是将摩尔比2：1的Fe³⁺与Fe²⁺盐在水溶液中同时水解沉淀，或Fe²⁺盐在 氧化剂存在条件下部分氧化沉淀实现Fe₃O₄纳米晶体的合成，共沉淀法具有方法 简单、成本低廉的优点。 但是共沉淀方法存在粒度分布宽、易团聚的缺点，而 且由于氧化铁与水之间反应较为复杂，可生成多种化合物，因此产物中常混入 其它相杂质，而不能充分发挥纳米氧化铁在生物体系中的作用。 经过改进的微 乳液法及超声空化法制备的纳米氧化铁，普遍存在结晶度差、磁性能低，及其 粒度、形貌难以控制的缺点。

[0007]

The synthesis of Fe₃O₄ or nanocrystals by high-temperature

decomposition and reduction of acetylacetone iron in high-boiling-point organic solvents is a successful synthetic method developed in recent years.

采用乙酰丙酮铁在高沸点有机溶剂中高温分解及还原生成Fe₃O₄或纳米晶 体，是近年发展的一个成功的合成方法。

The iron oxide nanoparticles synthesized by this method have the advantages of small particle size, uniform size and highly uniform dispersion (the particles are observed to be monodisperse under TEM electron microscopy, with little or no agglomeration). Sun Shouheng et al. used iron acetylacetone (Fe(acac)₃, each acetylacetone group containing two carbonyl groups) in diphenyl ether solvent to react with hexadecanediol, oleic acid, and oleylamine to generate Fe₃O₄ nanocrystals with a particle size of less than 20 nm (Journal of the American Chemical Society, 2002, 124, 8204-8205). Iron oxide nanocrystals obtained by this method have long alkyl chains or other small molecules of the organic solvent used on their surface. They can only be dissolved or dispersed in nonpolar or weakly polar organic solvents and cannot be used in the biomedical field at the scale of individual particles. Hydrophilicity on the surface of nano-iron oxide particles can only be achieved through the substitution of modifiers. The substitution process is complex and not conducive to practical applications. Gao Mingyuan (Chemistry of Materials, 2004, 16, 1391-1393, Chinese Patent Application No. 03136273.7: A method for preparing biocompatible

magnetic nanoparticles) et al. developed a method for the thermal decomposition of iron acetylacetonate in high-boiling-point solvents. They used strongly polar solvents such as 2-pyrrolidone as the reaction heat transfer medium and coordination solvent, and obtained water-soluble Fe₃O₄ nanoparticles through a one-step reaction method. In order to prepare biocompatible nanoparticles that are stably dispersed in neutral water, a displacement reaction must be used to replace the organic solvents such as pyrrolidone adsorbed on the surface of the iron oxide nanoparticles, but there are cases where the displacement is incomplete. Jiaqi Wan and Wei Cai et al. (Chemical Communications, 2007, 5004-5006) and Dipak Maity (Journal of Magnetics and Magnetic Materials, 2009, 321, 3093-3098) prepared water-soluble Fe₃O₄ nanoparticles by high-temperature decomposition of acetylacetone iron in triethylene glycol (TREG), an organic small molecule with good water solubility. However, the prepared Fe₃O₄ nanoparticles did not exhibit high stability in water.

该方法合成的氧化铁纳米粒子具有粒 度小、尺寸均一及高度均匀分散(TEM电镜下观察粒子呈单分散状态，没有或极 少团聚)的优点。 Sun Shouheng等采用在二苯醚溶剂中，乙酰丙酮铁(Fe(acac)₃ 每个乙酰丙酮集团含两个羰基)与十六烷二醇、油酸、油胺作用生成粒径小于 20nm的Fe₃O₄纳米晶体(Journal of the American Chemical Society，2002，124， 8204～8205)。 这类方法得到的氧化铁纳米晶体，表面修饰有长烷基链或其它所 使用的有机溶剂小分子，只能溶解或分散于非极性或弱极性的有机溶剂中，不 能在单个微粒尺度上被用于生物

医学领域。 必须通过修饰体置换才可以使纳米 氧化铁粒子表面具有亲水性，置换过程复杂，不利于实际应用。 高明远 (Chemistry of Materials，2004，16，1391～1393，中国专利申请号03136273.7： 一种制备具有生物相容性的磁性纳米微粒的方法)等发展了乙酰丙酮铁在高沸 点溶剂中热分解方法，采用2-吡咯烷酮等一类强极性溶剂作为反应传热介质和 配位溶剂，通过一步反应法得到了具有水溶性的纳米Fe₃O₄纳米粒子。 为了制备 在中性水中稳定分散的生物相容性纳米粒子，也必须采用置换反应将氧化铁纳 米粒子表面吸附的吡咯烷酮等有机溶剂替代，存在置换不完全的情况。 Jiaqi Wan和Wei Cai等(Chemical communications，2007，5004-5006)，及Dipak Maity(Journal of magnetism and magnetic materials，2009，321，3093～3098)等人利用在具有良好水溶性的有机小分子三甘醇(TREG)中高温分解乙 酰丙酮铁制备了水溶性的纳米Fe₃O₄粒子，但是制备的纳米Fe₃O₄粒子在水中的稳 定性不高。

Ricardo H. Goncalves (Journal of Materials Chemistry, 2010, 20, 1167-1172) et al. decomposed acetylacetone iron in PEG of different molecular weights to prepare water-soluble nano Fe₃O₄ particles. However, the synthesized nano Fe₃O₄ particles easily combined with each other and quickly formed a precipitate in water.

Ricardo H.Goncalves(Journal of Materials Chemistry，2010， 20，1167～1172)等人在不同分子量的PEG中分解乙酰丙酮铁，制备了水溶性的 纳米Fe₃O₄粒子，但是合成的纳米Fe₃O₄粒子之间容易相互结合，在水中很快形成 沉淀。

[0008]

Summary of the Invention

发明内容

[0009]

The purpose of this invention is to provide a method for preparing magnetic iron oxide nanoparticles that can be stably dispersed in water.

本发明的目的是提供一种能稳定分散于水中的磁性氧化铁纳米粒子的制备 方法。

[0010]

The specific steps are as follows:

具体步骤为：

[0011]

Weigh 10–30 g of triethylene glycol (TREG) or polyethylene glycol (PEG) with a molecular weight of 600–20000 or polyethylene glycol monomethyl ether (MPEG) with a molecular weight of 600–20000, add 0.15–3 g of additives, and place the above raw materials into a three-

necked flask. Heat the flask to 70–90°C on a temperature-controlled magnetic stirrer, then add 0.1–3 g of analytical grade ferric acetylacetone. Stir with a magnetic stirrer for 5–15 minutes, with flowing argon gas for protection during heating. Then raise the temperature to 150–320°C and heat for 20–600 minutes. The solution will change from red to black. After stopping heating, let the solution cool to below 60°C, add 50–70 ml of analytical grade toluene or acetone, and separate the black precipitate by magnetic adsorption. Wash twice with analytical grade acetone to remove excess impurities. Organic matter, the precipitate was dissolved in water to obtain magnetic iron oxide Fe₃O₄ nanoparticles with a particle size of 3-50 nanometers;

称取10～30克三甘醇(TREG)或分子量从600～20000的聚乙二醇(PEG) 或分子量从600～20000的聚乙二醇单甲醚(MPEG)，加入0.15～3克添加剂，将 以上原料装入三口烧瓶中，置于控温磁力搅拌器上加热至70～90°C，再加入0.1～ 3克分析纯乙酰丙酮铁，用磁力搅拌子搅拌5～15分钟，加热过程中通以流动氩 气保护，然后再升温至150～320°C，加热20～600分钟，溶液由红色变为黑色， 停止加热后，待溶液冷却到60°C以下，加入50～70ml分析纯甲苯或丙酮，通 过磁铁吸附将黑色沉淀物分离出来，再用分析纯丙酮清洗两次以除去多余的有 机物，将沉淀溶解于水中，得到粒径在3～50纳米的磁性氧化铁Fe₃O₄纳米粒子；

[0012]

The additive is one of polyethyleneimine (PEI) with a molecular weight between 800 and 100,000, polyvinylpyrrolidone (PVP) with a molecular weight between 800 and 100,000, and sodium alkyl sulfate with a carbon chain length between 8 and 20.

所述添加剂为分子量在800～100000之间的聚乙烯亚胺(PEI)、分子量在 800～100000之间的聚乙烯吡咯烷酮(PVP)和碳链长度在8～20之间的烷基硫 酸钠中的一种。

[0013]

This invention can prepare magnetic iron oxide Fe₃O₄ nanoparticles that are stably dispersed in water. The entire reaction process is simple and controllable and easy to put into production.

本发明可以制备稳定分散于水中的磁性氧化铁Fe₃O₄纳米粒子，整个反应过 程简单可控，容易投入生产。

The prepared magnetic iron oxide Fe₃O₄ nanoparticles can be used in fields such as biology, medicine, catalysis and mechanical lubrication.

所制备的磁性氧化铁Fe₃O₄纳米粒子可以用于生物、 医药、催化及机械润滑等领域。

[0014]

Attached Figure Description

附图说明

[0015]

Figure 1 is a transmission electron microscope (TEM) image of the nanoparticles prepared in Example 1 of the present invention.

图1为本发明实施例1制备的纳米粒子的透射电镜(TEM)形貌照片。

[0016]

Figure 2 is a transmission electron microscope (TEM) image of the nanoparticles prepared in Example 2 of the present invention.

图2为本发明实施例2制备的纳米粒子的透射电镜(TEM)形貌照片。

[0017]

Figure 3 is a transmission electron microscope (TEM) image of the nanoparticles prepared in Example 3 of this invention.

图3为本发明实施例3制备的纳米粒子的透射电镜(TEM)形貌照片。

[0018]

Figure 4 shows a transmission electron microscope (TEM) image of the nanoparticles prepared in Example 4 of this invention.

图4为本发明实施例4制备的纳米粒子的透射电镜(TEM)形貌照片。

[0019]

Figure 5 shows a transmission electron microscope (TEM) image of the nanoparticles prepared in Example 5 of this invention.

图5为本发明实施例5制备的纳米粒子的透射电镜(TEM)形貌照片。

[0020]

Figure 6 shows a transmission electron microscope (TEM) image of the nanoparticles prepared in Example 6 of this invention.

图6为本发明实施例6制备的纳米粒子的透射电镜(TEM)形貌照片。

[0021]

Detailed Implementation

具体实施方式

[0022]

Example 1:

实施例1：

[0023]

Weigh 15.1g of PEG (molecular weight 1000) and add 0.11g of PEI (molecular weight 1800).

称取15.1g PEG(分子量为1000)，加入0.11克PEI(分子量1800)。

The above raw materials were placed in a three-necked flask and heated to 80°C on a temperature-controlled magnetic stirrer. Then, 0.72 g of analytical grade acetylacetone iron was added, and the mixture was stirred with a magnetic stir bar for 10 minutes. During the heating process, a flowing argon gas was passed through for protection. Then, the temperature was raised to 260°C and heated for 60 minutes. The solution changed from red to black.

将以上 原料装入三口烧瓶中，置于控温磁力搅拌器上加热至80°C，再加入0.72克分析 纯乙酰丙酮铁，用磁力搅拌子搅拌10分钟，加热过程中通以流动氩气保护，然 后再升温至260°C，加热60分钟，溶液由红色变为黑色。

After heating is stopped, wait for the solution to cool to below 60°C, add 60 ml of analytical grade toluene, and separate the black precipitate by magnetic adsorption. Then wash twice

with analytical grade acetone to remove excess organic matter, and dissolve the precipitate in water.

停止加热后，待溶液 冷却到60°C以下，加入60ml分析纯甲苯，通过磁铁吸附将黑色沉淀物分离出来，再用分析纯丙酮清洗两次以除去多余的有机物，将沉淀溶解于水中。

The electrophoretic particle size of this nanoparticle is 28 nm.

该纳 米粒子的电泳粒度为28nm。

The morphology of the nanoparticles was observed using transmission electron microscopy (TEM). Figure 1 shows a TEM image of the magnetic nanoparticles, which reveals an average grain size of 15 nm.

用透射电镜(TEM)观察纳米粒子形貌，图1为该磁 性纳米粒子的透射电镜照片，从电镜照片中可以看到晶粒平均粒径为15nm。

The nanoparticles have a zeta potential of +25 mV in aqueous solution.

该 纳米粒子在水溶液中Zeta电位为+25mV。

Thermogravimetric analysis revealed that the surface of the nanoparticles contained approximately 43% organic matter.

经热重分析纳米粒子表面含有约43% 的有机物。

X-ray diffraction analysis results indicate that the product is a Fe₃O₄ crystalline phase.

X衍射分析结果表明产物为Fe₃O₄晶相。

The saturation magnetization of the nanoparticle was measured to be 79 emu/g Fe₃O₄ (calculated after removing the weight of organic matter) using a superconducting quantum interference device (Squid), and it also exhibits superparamagnetism.

用超导量子干涉仪Squid测 定该纳米粒子的饱和磁化强度为79emu/g Fe₃O₄(除去有机物重量后计算所得量 值)，并具有超顺磁性。

When the product is dissolved in water, a dispersed suspension can be formed. Because the amount of PEI added to the reactants is small, a precipitate appears after one day.

将产物溶解于水中，可以形成分散的悬浮液，因反应物 中添加PEI量少，放置一天后有沉淀出现。

[0024]

Example 2:

实施例2：

[0025]

Weigh 15.3g of PEG (molecular weight 1000) and add 0.31g of PEI (molecular weight 1800).

称取15.3g PEG(分子量为1000)，加入0.31克PEI(分子量1800)。

The above raw materials were placed in a three-necked flask and heated to 80°C on a temperature-controlled magnetic stirrer. Then, 0.72 g of analytical grade acetylacetone iron was added, and the mixture was stirred with a magnetic stir bar for 10 minutes. During the heating process, a flowing argon gas was passed through for protection. Then, the temperature was raised to 260°C and heated for 60 minutes. The solution changed from red to black.

将以上 原料装入三口烧瓶中，置于控温磁力搅拌器上加热至80°C，再加入0.72克分析 纯乙酰丙酮铁，用磁力搅拌子搅拌10分钟，加热过程中通以流动氩气保护，然 后再升温至260°C，加热60分钟，溶液由红色变为黑色。

After heating is stopped, wait for the solution to cool to below 60°C, add 60 ml of analytical grade toluene, and separate the black precipitate by magnetic adsorption. Then wash twice

with analytical grade acetone to remove excess organic matter, and dissolve the precipitate in water.

停止加热后，待溶液 冷却到60°C以下，加入60ml分析纯甲苯，通过磁铁吸附将黑色沉淀物分离出来，再用分析纯丙酮清洗两次以除去多余的有机物，将沉淀溶解于水中。

The average electrophoretic particle size of this nanoparticle is 27 nm.

该纳 米粒子的电泳粒度平均为27nm。

The morphology of the nanoparticles was observed using transmission electron microscopy (TEM). Figure 2 shows a TEM image of the magnetic nanoparticles, which reveals an average grain size of 20 nm.

用透射电镜(TEM)观察纳米粒子形貌，图2为 该磁性纳米粒子的透射电镜照片，从电镜照片中可以看到晶粒平均粒径为20nm。

The nanoparticle has a zeta potential of +32 mV in aqueous solution.

该纳米粒子在水溶液中Zeta电位为+32mV。

Thermogravimetric analysis revealed that the surface of the nanoparticles contained approximately 33% organic matter.

经热重分析纳米粒子表面含有约33% 的有机物。

X-ray diffraction analysis results indicate that the product is of the Fe₃O₄ crystalline phase.

X衍射分析结果表明产物为Fe₃O₄晶相。

The saturation magnetization of the nanoparticle was measured using a superconducting quantum interference device (Squid) to be 81 emu/g Fe₃O₄ (the value calculated after removing the weight of organic matter), and it exhibits superparamagnetism. When the product is dissolved in water, it forms a stable and dispersed suspension, and no precipitate forms after being left for more than 40 days.

用超导量子干涉仪Squid测 定该纳米粒子的饱和磁化强度为81emu/g Fe₃O₄(除去有机物重量后计算所得量 值)，并具有超顺磁性。 将产物溶解于水中，可以形成稳定分散的悬浮液，并且 放置40天以上未形成沉淀。

[0026]

Example 3:

实施例3：

[0027]

Weigh 15.2g of PEG (molecular weight 1000) and add 0.51g of PEI (molecular weight 1800).

称取15.2g PEG(分子量为1000)，加入0.51克PEI(分子量1800)。

The above raw materials were placed in a three-necked flask and heated to 80°C on a temperature-controlled magnetic stirrer. Then, 0.73 g of analytical grade acetylacetone iron was added, and the mixture was stirred with a magnetic stir bar for 10 minutes. During the heating process, a flowing argon gas was passed through for protection. Then, the temperature was raised to 260°C and heated for 60 minutes. The solution changed from red to black.

将以上 原料装入三口烧瓶中，置于控温磁力搅拌器上加热至80°C，再加入0.73克分析 纯乙酰丙酮铁，用磁力搅拌子搅拌10分钟，加热过程中通以流动氩气保护，然 后再升温至260°C，加热60分钟，溶液由红色变为黑色。

After heating is stopped, wait for the solution to cool to below 60°C, add 60 ml of analytical grade toluene, and separate the black precipitate by magnetic adsorption. Then wash twice with analytical grade acetone to remove excess organic matter, and dissolve the precipitate in water. The average electrophoretic particle size of this nanoparticle is 30 nm. The morphology of the nanoparticles was observed using transmission electron microscopy (TEM). Figure 3 shows a TEM image of the magnetic nanoparticles, which reveals an average grain size of 21 nm. The nanoparticles have a zeta potential of +35 mV in aqueous solution.

Thermogravimetric analysis revealed that the surface of the nanoparticles contained approximately 31% organic matter. X-ray diffraction analysis results indicate that the product is of the Fe₃O₄ phase. The saturation magnetization of the nanoparticle was measured to be 73 emu/g Fe₃O₄ (calculated after removing the weight of organic matter) using a superconducting quantum interference device (Squid), and it also exhibits superparamagnetism. When the product is dissolved in water, it forms a dispersed suspension, and no precipitate forms after being left for more than 40 days.

停止加热后，待溶液 冷却到60°C以下，加入60ml分析纯甲苯，通过磁铁吸附将黑色沉淀物分离出来，再用分析纯丙酮清洗两次以除去多余的有机物，将沉淀溶解于水中。 该纳 米粒子的电泳粒度平均为30nm。 用透射电镜(TEM)观察纳米粒子形貌，图3为 该磁性纳米粒子的透射电镜照片，从电镜照片中可以看到晶粒平均粒径为21nm。 该纳米粒子在水溶液中Zeta电位为+35mV。 经热重分析纳米粒子表面含有约31% 的有机物。 X衍射分析结果表明产物为Fe₃O₄晶相。 用超导量子干涉仪Squid测 定该纳米粒子的饱和磁化强度为73emu/g Fe₃O₄(除去有机物重量后计算所得量 值)，并具有超顺磁性。 将产物溶解于水中，可以形成分散的悬浮液，并且放置 40天以上未形成沉淀。

[0028]

Example 4:

实施例4：

[0029]

Weigh 15.4g of PEG (molecular weight 1000) and add 1.1g of PEI (molecular weight 1800).

称取15.4g PEG(分子量为1000)，加入1.1克PEI(分子量1800)。

The above raw materials were placed in a three-necked flask and heated to 80°C on a temperature-controlled magnetic stirrer. Then, 0.72 g of analytical grade acetylacetone iron was added, and the mixture was stirred with a magnetic stir bar for 10 minutes. During the heating process, a flowing argon gas was passed through for protection. Then, the

temperature was raised to 260°C and heated for 30 minutes. The solution changed from red to black.

将以上 原料装入三口烧瓶中，置于控温磁力搅拌器上加热至80°C，再加入0.72克分析 纯乙酰丙酮铁，用磁力搅拌子搅拌10分钟，加热过程中通以流动氩气保护，然 后再升温至260°C，加热30分钟，溶液由红色变为黑色。

After heating is stopped, wait for the solution to cool to below 60°C, add 60 ml of analytical grade toluene, and separate the black precipitate by magnetic adsorption. Then wash twice with analytical grade acetone to remove excess organic matter. The electrophoretic particle size of the nanoparticle is 21 nm. The morphology of the nanoparticles was observed using transmission electron microscopy (TEM). Figure 4 shows a TEM image of the magnetic nanoparticles, which shows that the average grain size is about 10 nm. The nanoparticles have a zeta potential of +41 mV in aqueous solution. Thermogravimetric analysis revealed that the surface of the nanoparticles contained approximately 16% organic matter. X-ray diffraction analysis results indicate that the product is a Fe₃O₄ crystalline phase. The saturation magnetization of the nanoparticle was determined to be 68 emu/g Fe₃O₄ (calculated after removing the weight of organic matter) using a superconducting quantum interference device (Squid), and it also exhibits

superparamagnetic properties. When the product is dissolved in water, it forms a dispersed suspension, and no precipitate forms after being left for more than 40 days.

停止加热后，待溶液 冷却到60°C以下，加入60ml分析纯甲苯，通过磁铁吸附将黑色沉淀物分离出来，再用分析纯丙酮清洗两次以除去多余的有机物。 该纳米粒子的电泳粒度为 21nm。 用透射电镜(TEM)观察纳米粒子形貌，图4为该磁性纳米粒子的透射电 镜照片，从电镜照片中可以看到晶粒平均粒径约为10nm。 该纳米粒子在水溶液 中Zeta电位为+41mV。 经热重分析纳米粒子表面含有约16％的有机物。 X衍射分 析结果表明产物为Fe₃O₄晶相。 用超导量子干涉仪Squid测定该纳米粒子的饱和 磁化强度为68emu/g Fe₃O₄(除去有机物重量后计算所得量值)，并具有超顺磁 性。 将产物溶解于水中，可以形成分散的悬浮液，并且放置40天以上未形成沉 淀。

[0030]

Example 5:

实施例5：

[0031]

Weigh 20.3g of PEG (molecular weight 1000) and add 0.71g of polyvinylpyrrolidone (PVP) (molecular weight 8000).

称取20.3g PEG(分子量为1000)，加入0.71克聚乙烯吡咯烷酮PVP(分子 量8000)。

The above raw materials were placed in a three-necked flask and heated to 80°C on a temperature-controlled magnetic stirrer. Then, 0.72 g of analytical grade acetylacetone iron was added, and the mixture was stirred with a magnetic stir bar for 10 minutes. During the heating process, a flowing argon gas was passed through for protection. The temperature was then raised to 260°C and heated for 60 minutes. The solution changed from red to black.

将以上原料装入三口烧瓶中，置于控温磁力搅拌器上加热至80°C， 再加入0.72克分析纯乙酰丙酮铁，用磁力搅拌子搅拌10分钟，加热过程中通 以流动氩气保护，然后再升温至260°C，加热60分钟，溶液由红色变为黑色。

After heating is stopped, the solution is allowed to cool to room temperature. 60 ml of analytical grade toluene is added, and the black precipitate is separated by magnetic adsorption. The solution is then washed twice with analytical grade acetone to remove excess organic matter. The morphology of the nanoparticles was observed using transmission electron microscopy (TEM). Figure 5 shows a TEM image of the magnetic nanoparticles, which shows that the average grain size is about 11.8 nm. The nanoparticle has a zeta potential of 0 mV in aqueous solution. The electrophoretic particle size of the nanoparticle is 39 nm. X-ray diffraction analysis results indicate that the product is of the Fe₃O₄ crystalline phase. Due to the steric hindrance formed by PVP and PEG together, the product can be dissolved in water to form a stable and dispersed suspension for a long time.

停止加热后，待溶液冷却到室温，加入60ml分析纯甲苯，通过磁铁吸附将黑色 沉淀物分离出来，再用分析纯丙酮清洗两次以除去多余的有机物。 用透射电镜 (TEM)观察纳米粒子形貌，图5为该磁性纳米粒子的透射电镜照片，从电镜照 片中可以看到晶粒平均粒径约为11.8nm。 该纳米粒子在水溶液中Zeta电位为 0mV。 该纳米粒子的电泳粒度为39nm。 X衍射分析结果表明产物为Fe₃O₄晶相。 因为PVP与PEG一起形成的空间位阻作用，将产物溶解于水中可以形成长时间 稳定分散的悬浮液。

[0032]

Example 6:

实施例6：

[0033]

Weigh 20.04g of triethylene glycol and add 0.32g of sodium dodecyl sulfate.

称取20.04g三甘醇，加入0.32克十二烷基硫酸钠。

The above raw materials were placed in a three-necked flask and heated to 80°C on a temperature-controlled magnetic stirrer. Then, 0.71 g of analytical grade acetylacetone iron was added, and the mixture was stirred with a magnetic stir bar for 10 minutes. During the

heating process, a flowing argon gas was passed through for protection. The temperature was then raised to 280°C and heated for 30 minutes. The solution changed from red to black.

将以上原料装入三口烧 瓶中，置于控温磁力搅拌器上加热至80°C，再加入0.71克分析纯乙酰丙酮铁， 用磁力搅拌子搅拌10分钟，加热过程中通以流动氩气保护，然后再升温至280°C， 加热30分钟，溶液由红色变为黑色。

After heating is stopped, wait for the solution to cool to below 60°C, add 60 ml of analytical grade acetone, and separate the black precipitate by magnetic adsorption. Then wash twice with analytical grade acetone to remove excess organic matter. The morphology of the nanoparticles was observed using transmission electron microscopy (TEM). Figure 6 shows a TEM image of the magnetic nanoparticles, which reveals an average grain size of 6.5 nm. X-ray diffraction analysis results indicate that the product is Fe₃O₄ crystalline phase. The saturation magnetization of the nanoparticles (Fe₃O₄nanoparticles containing organic matter) was determined to be 52 emu/g using a superconducting quantum interference device (Squid), and the nanoparticles exhibit superparamagnetism. However, the prepared product is insoluble in water. 5.08 g of the original reaction solution was washed with analytical grade acetone, adsorbed with a magnet and precipitated. The precipitate was added to 8 mL of chloroform to prepare a Fe₃O₄ solution with a concentration of 5 mg/mL. Then, 50 mL of

dimethyl sulfoxide (DMSO) and 0.54 g of PEI were added, and the mixture was stirred at room temperature for 48 h. The liquid was then washed with analytical grade acetone and precipitated using a magnet. The precipitate was then stably dispersed in deionized water.

停止加热后，待溶液冷却到60°C以下， 加入60ml分析纯丙酮，通过磁铁吸附将黑色沉淀物分离出来，再用分析纯丙酮 清洗两次以除去多余的有机物。 用透射电镜(TEM)观察纳米粒子形貌，图6为 该磁性纳米粒子的透射电镜照片，从电镜照片中可以看到晶粒平均粒径为 6.5nm。 X衍射分析结果表明产物为Fe₃O₄晶相。 用超导量子干涉仪Squid测定 该纳米粒子的饱和磁化强度为52emu/g(含有机物的Fe₃O₄纳米粒子)，并具 有超顺磁性。 但是所制备的产物不溶解于水，将5.08g的反应原液用分析纯丙 酮清洗，磁铁吸附并使其沉淀，取沉淀物加入到8mL的氯仿配成浓度在5mg/mL 的Fe₃O₄溶液，之后加入50mL二甲亚砜(DMSO)和0.54g的PEI，并在室温下搅 拌48h。 之后将液体用分析纯丙酮清洗并用磁铁吸附并使其沉淀，该沉淀能够稳 定地分散于去离子水中。