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An approach to give prospective life-span of the copper/low-density-polyethylene nanocomposite intrauterine device

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Abstract As a novel copper-containing intrauterine device (IUD), the prospective life-span of the copper/low-density-polyethylene (Cu/LDPE) nanocomposite IUD is very important for the future clinical use and should be given in advance. Here a novel approach, cupric ions accelerated release in diluted nitric acid solution and cupric ions concentration release in various volume of simulated uterine solution (SUS), is reported to verify the type of cupric ions release model of the cylindrical matrix-type nanocomposite IUD, and to obtain the minimal cupric ions release rate that need to ensure contraceptive efficacy and the thickness of copper particles exhausted layer of the cylindrical matrix-type nanocomposite IUD within two difficult immersion durations in experimental volume of SUS, respectively. Using these results, the prospective life-span of the cylindrical matrix-type nanocomposite IUD can be obtained. For instance, the prospective life-span of the novel γ-shape nanocomposite IUD with 25 wt% of copper nanoparticles and 2 mm of diameter and a total weight of 285 mg can be given in advance and it is about 5 years in the future clinical use.

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1 Introduction

Copper-containing intrauterine device (Cu-IUD) is one of the worldwide used forms for birth control. According to report [1] of the National Population and Family Planning Commission of China, about 114 millions of Chinese reproductive females are IUD users in 2006. However, such side effects as pain, bleeding and spotting that caused by the existing Cu-IUD has not been overcome in clinical use [2, 3]. Factors that result in these side effects have been summarized in one of our previous paper [4], i.e., the fragmentation of copper wire or copper sleeve after long-term corrosion in uterine secretions [5], the burst release of cupric ions within first few months after insertion [6, 7], the direct contact between copper and endometrium [8], the more and more rough surface of copper after long-term use [9, 10] and so on. To eliminate these adverse factors of the existing Cu-IUD, copper/low-density-polyethylene (Cu/LDPE) nanocomposite IUD has been developed. As a novel substitute, the nanocomposite IUD has the same excellent contraceptive efficacy as that of the existing Cu-IUD, and it can lessen such side effects as pain, bleeding and spotting that existed in the existing Cu-IUD remarkably [11].

In the future clinical use, prospective life-span of the nanocomposite IUD, which is one of the most important properties of Cu-IUD, must be given in advance. However, Cu-IUD can usually be used effectively for 5–10 years [12], and serum albumin, which is one of the most important compositions of simulated uterine solution (SUS), will begin to decay after 48 h at temperature of 37.0 ± 0.5°C [13]. Therefore, it is not easy to give the prospective life-span of nanocomposite IUD in advance. To obtain the prospective life-span of nanocomposite IUD for the future clinical use, the following problems should be resolved firstly: the type of cupric ions release model of nanocomposite IUD and the minimal cupric ions concentration in experimental volume of SUS that needs to ensure contraceptive efficacy.

The Cu/LDPE nanocomposite is a hybrid of LDPE matrix and copper nanoparticles [14]. Its copper nanoparticles, which are dispersed homogeneously in the LDPE matrix, will convert into cupric ions when they met with aqueous solutions such as water and SUS [13, 15, 16]. When the cupric ions released and dissolved in uterine secretions, they can lead the spermatozoa to lose their activities [17] and enhance the contraceptive efficacy of Cu-IUD. Out of question, the Cu/LDPE nanocomposite IUD is a matrix-type drug delivery system. For a cylindrical matrix-type drug delivery system, its drug release model has been established by many researchers [18, 19]. If the novel γ-shape nanocomposite IUD is belongs to a kind of cylindrical matrix-type drug delivery system, its cupric ions release mathematic model can be obtained. However, whether the γ-shape nanocomposite IUD is really a kind of cylindrical matrix-type drug delivery system or not needs to be verified by experiment.

In addition, the volume of SUS that used usually to immerse each of the nanocomposite IUD samples in our experiment is 50 ml, but the volume of uterine fluid, which might consist of cervical mucus plus endometrial secretions, of each potential nanocomposite IUD users is less than 1.0 ml [20, 21]. The relationship between cupric ions concentration released by the nanocomposite IUD in 50 ml of SUS and that in 1.0 ml of SUS is not clear, thus the minimal released cupric ions concentration in 50 ml of SUS that needs to ensure contraceptive efficacy of the nanocomposite IUD can not be obtained.

To resolve these problems, a novel approach, cupric ions accelerated release in diluted nitric acid solution and cupric ions concentration released in various volumes of SUS, is used in the present study. The aim of cupric ions accelerated release in diluted nitric acid solution is to determine the type of the cupric ions release model of nanocomposite IUD as soon as possible, the aim of cupric ions concentration release in various volumes of SUS is to obtain the minimal cupric ions concentration that needs to ensure contraceptive efficacy of the nanocomposite IUD in 50 ml of SUS. Additionally, the thickness of copper particles exhausted layer of the nanocomposite IUD in SUS within two difficult immersion durations can also be obtained by the experiment of cupric ions concentration released in various volumes of SUS. Using these results, the prospective life-span of nanocomposite IUD can be predicted in short-term, and it will make an important contribution to the future clinical application.

2 Materials and methods

2.1 Materials

The LDPE (melt index at 463 K/2.16 kg is 1.8–3.2 g/10 min) was bought as pellets from Qilu Petrochemical Corporation of China, and was grinded into micro-sized powder with an average particles size of 250 μm. The copper nanoparticles were prepared via our own patent techniques, i.e. hybrid induction and laser heating (HILH) evaporation condensation method [22], its mean diameter is about 50 nm, and the purity is no less than 99.9%.

2.2 Preparation of the Cu/LDPE nanocomposite IUD

The Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles was prepared by using the following process: firstly, running the Injection Molding Extruder (SA600/100, made in Ningbo Haitian Group Co. Ltd., China) and setting parameters of injection; secondly, mixing mixture of the LDPE powders and the copper nanoparticles in a tumble mixer for 10 min, and a homogeneous mixture was obtained; after the temperature was heated to 160, 180, 180 and 140°C from die to hopper for 30 min, putting the mixed powders into the hopper of Injection Molding Extruder and beginning to inject, and the samples of Cu/LDPE nanocomposite IUD in the shape of γ as shown in Fig. 1 are obtained.

The γ-shaped Cu/LDPE nanocomposite IUD have a pair of symmetrical transverse arms with total length of 30 mm

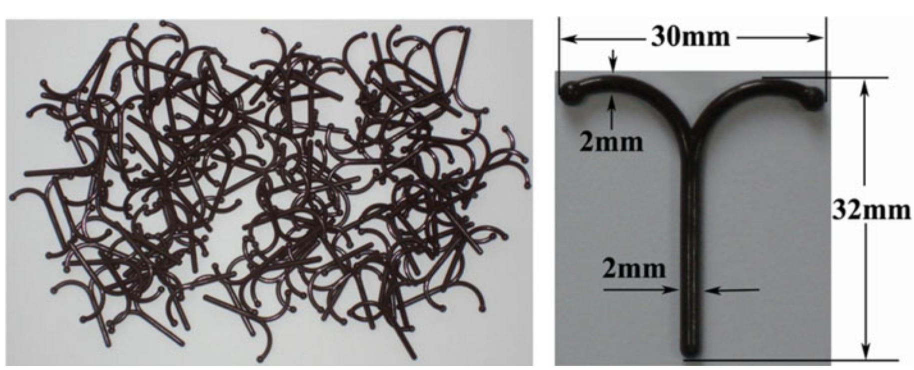

Fig. 1 Dimension of the novel γ-shaped Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles (unit after the numeral in the figure is mm)

and a longitudinal stem with total height of 32 mm, both the transverse arms and the longitudinal stem have a same diameter of 2.0 mm. In addition, the diameter of the hemispheroidal end of each transverse arm is 2.5 mm and that of the longitudinal stem is 2.0 mm. The mean weight of each γ-shaped Cu/LDPE nanocomposite IUD is about 285 mg.

2.3 Cupric ions accelerated release of the Cu/LDPE nanocomposite IUD

Fifteen samples of the γ-shaped nanocomposite IUD were taken out and divided into three groups, i.e., each group consist of five samples. All samples of the first group were put into a conical flask with 200 ml of diluted nitric acid solution, which consist of 160 ml of distilled water and 40 ml of nitric acid, then the conical flask was closed with a polished stopple and put into a water tank with a constant temperature of 37.0 ± 0.5°C. 120 days later, all samples of the second group were treated in the same way. After samples of the second group were immersed into the diluted nitric acid solution for 120 days, all samples of the first and the second groups were taken out and washed with distilled water, then dried with filter paper and denoted as NC-240 and NC-120, respectively. That is, samples of NC-240 and NC-120 were immersed into the diluted nitric acid solution for 240 days and 120 days, respectively. The five samples of the third group that were not immersed into the diluted nitric acid solution were denoted as NC-000. Appearances of these three types of experimental samples were presented in Fig. 2.

All these experimental samples were prepared for scanning electron microscopy (SEM) observation and X-ray energy dispersive spectroscopy (EDS) analysis.

2.4 SEM observation and EDS analysis of the experimental samples

Two samples were taken at random out of each group of the experimental Cu/LDPE nanocomposite IUD (include NC-000, NC-120 and NC-240) and used for the preparation of specimens for SEM observation and EDS analysis. One sample of each group was used for the preparation of specimen for structure observation and copper radial distribution analysis, this kind of specimen was obtained by cooling the longitudinal stem of the chosen samples in liquid nitrogen for about 5 min and then broken into pieces. Another sample of each group was used for the preparation of specimen for morphology observation and copper whole area distribution analysis, this kind of specimen was obtained by cutting the longitudinal stem of the chosen samples into pieces. All these specimens were gilded before they were observed. SEM observation was carried out on a Quanta 200 scanning electron microscopy (FEI, USA) at an acceleration voltage of 20 kV, and EDS analysis was performed with the same equipment.

2.5 Cupric ions release of the nanocomposite IUD in various volume of SUS

Eight samples were taken at random out of the prepared γ-shaped nanocomposite IUD, and each of them was put into a conical flask with SUS with volume of 5, 10, 15, 20, 25, 30, 40 and 50 ml, respectively. The composition (g/l) of the SUS is used as follows [6, 23, 24]: 4.97 NaCl, 0.224 KCl, 0.167 $CaCl_2$, 0.25 $NaHCO_3$, 0.50 Glucose, 0.072 $NaH_2PO_4 \cdot 2H_2O$ and 0.5 Serum albumin. Experiments were performed at a constant temperature of 37.0 ± 0.5°C. Twenty-four hours later, the cupric ions concentration in the SUS was measured by using absorbance measurements [16, 24] with a UV-2102PC spectrophotometer (PerkinElmer Instruments (Shanghai) Co., LTD). To avoid retarding cupric ions release, the SUS was replaced by a freshly prepared batch once a week, and the cupric ions concentration in the SUS was measured again after 24 h of incubation.

2.6 Prediction of the life-span of nanocomposite IUD

The type of cupric ions release model of the nanocomposite IUD can be verified from the results of SEM observation and EDS analysis of the experimental samples that were

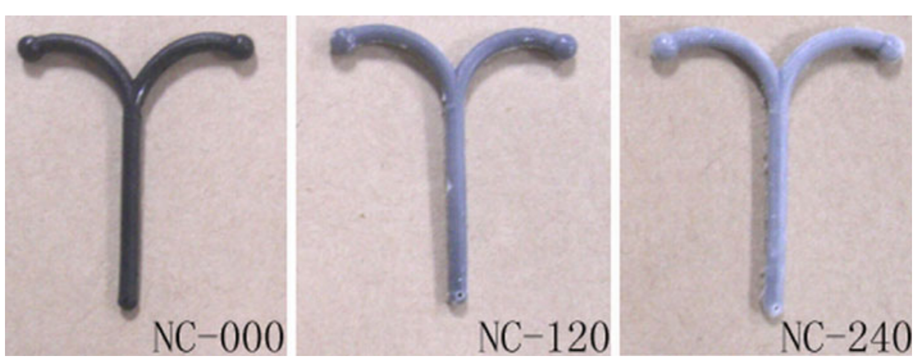

Fig. 2 Appearances of the novel γ-shaped Cu/LDPE nanocomposite IUD immersed in diluted nitric acid solution for various durations (NC-000 is for 0 day, NC-120 is for 120 day, NC-240 is for 240 day, respectively)

immersed into the diluted nitric acid solution for various duration. Apparently, the various immersion media will change the cupric ions release rate but will not change the cupric ions release model of the nanocomposite IUD, thus the cupric ions release model of the nanocomposite IUD immersed into SUS is similar to that immersed into diluted nitric acid solution. Combining with the thickness of copper particles exhausted layer of the nanocomposite IUD in SUS within two difficult immersion durations, the cupric ions release mathematical model of the nanocomposite IUD in SUS can be established. In addition, the minimal released cupric ions concentration that need to ensure contraceptive efficacy of the nanocomposite IUD in 50 ml of SUS can be obtained from the relationship between the released cupric ions concentration and the volume of SUS. Using these results, the prospective life-span of nanocomposite IUD can be predicted.

3 Results and discussion

3.1 Appearance of the experimental nanocomposite IUD

Appearances of the nanocomposite IUD immersed in diluted nitric acid solution for various durations were shown in Fig. 2. It can be seen that color of the original nanocomposite IUD (NC-000 in Fig. 2) is black, colors of the nanocomposite IUD immersed in diluted nitric acid solution are light black (NC-120 and NC-240 in Fig. 2), and the longer the immersion duration is, the lighter the color of the immersed samples is.

The Cu/LDPE nanocomposite is a hybrid of LDPE matrix and copper nanoparticles, the copper nanoparticles is black and the LDPE is white, thus the original Cu/LDPE nanocomposite IUD is black as that shown in Fig. 1. After the original nanocomposite IUD was put into diluted nitric acid solution or SUS, the following process will take out: firstly, the media enters into the nanocomposite IUD through the interspaces among the molecular chains and the pores existed in the nanocomposite IUD; secondly, the copper particles react with the entered media and convert into cupric ions, and a cupric ions concentration grads was formed, the cupric ions concentration grads is the diffusion motility of the cupric ions; finally, the cupric ions inside the nanocomposite IUD diffuse into the ambient media around the nanocomposite IUD. Resulting in the color of the nanocomposite IUD becomes lighter and lighter with the increasing of immersion duration as that shown in Fig. 2.

3.2 Structure and copper distribution of the experimental nanocomposite IUD

SEM image of the brittle fracture surface of the novel γ-shaped Cu/LDPE nanocomposite IUD after immersed in diluted nitric acid solution for 240 days were presented in Fig. 3. It can be seen that two kind of different area, which are easy to distinguish by interface as shown by dot line, was formed in the brittle fracture surface of the nanocomposite IUD after immersed in diluted nitric acid solution; from the amplification figure of the outer layer as shown in the upper right corner in Fig. 3, it can be seen that the copper particles were disappeared already; from the

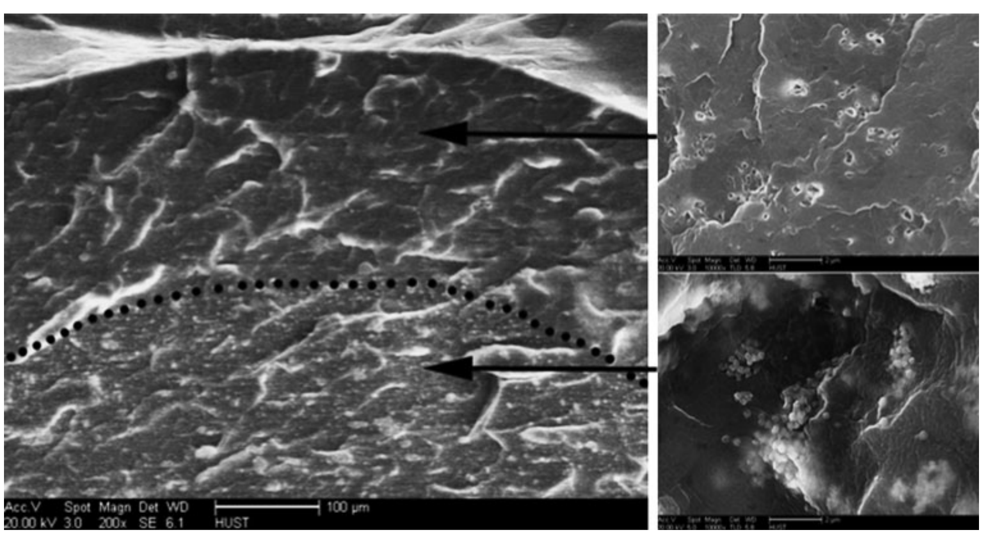

Fig. 3 SEM image of the brittle fracture surface of the novel γ-shaped Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles after immersed in diluted nitric acid solution for 240 days

amplification figure of the inner layer as shown in the lower right corner in Fig. 3, it can be seen that the copper particles were still existed.

EDS radial distribution of copper cross the brittle fracture surface of the novel γ-shaped Cu/LDPE nanocomposite IUD after immersed in diluted nitric acid solution for 240 days were given in Fig. 4. It can be seen that the amount of copper particles existed in the inner layer of the nanocomposite IUD is much larger than that existed in its outer layer, indicating that this result is in perfect agreement with the result obtained from Fig. 3.

SEM images and EDS whole area copper profiles of the cross-section of the novel γ-shaped Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles after immersed in diluted nitric acid solution for various durations were presented in Fig. 5. It can be seen that thickness of copper particles exhausted layer of the nanocomposite IUD, which can be estimated by using the distance from the outmost layer to the dot line as drawn around the interface, increase with the increasing of immersion duration in diluted nitric acid solution, i.e., the longer the immersion duration is, the thicker the thickness of copper particles exhausted layer is.

After the original nanocomposite IUD was put into diluted nitric acid solution or SUS, the copper particles inside the polymer will convert into cupric ions and the cupric ions will diffuse into the ambient media around the nanocomposite IUD, thus a copper particles exhausted layer was formed as that shown in Fig. 3, and a type of radial copper distribution was created as what presented in Fig. 4. Furthermore, with increasing of the immersion duration, the thickness of copper particles exhausted layers become larger as those shown in Fig. 5.

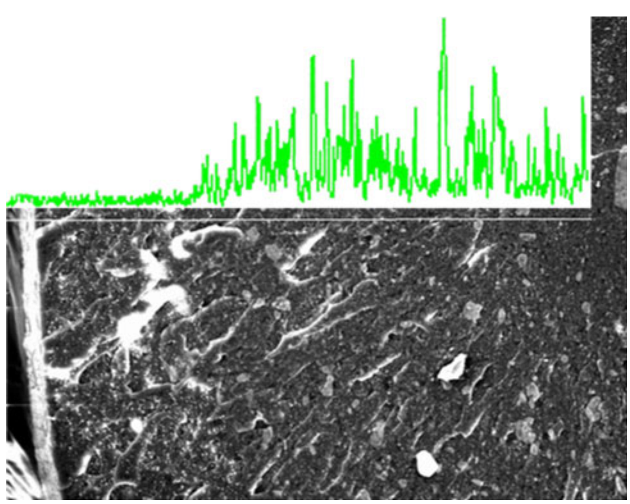

Fig. 4 EDS radial distribution of copper cross the brittle fracture surface of the novel γ-shaped Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles after immersed in diluted nitric acid solution for 240 days

3.3 Cupric ions release mode of the nanocomposite IUD

From the results of appearances, structure and copper distribution of the novel γ-shaped nanocomposite IUD immersed in diluted nitric acid solution for various durations, it can be seen that the thickness of copper particles exhausted layer changes with the increasing of immersion duration and it can be illustrated as these presented in Fig. 6. Indicating that the novel γ-shaped Cu/LDPE nanocomposite IUD is really a cylindrical matrix-type drug delivery system, and its cupric ions release obeys the release model of cylindrical matrix-type drug delivery system.

Mathematical modeling of cupric ions release of the γ-shaped Cu/LDPE nanocomposite IUD is illustrated in Fig. 7. Here r_0 is radius of either the transverse arms or the longitudinal stem, r_1 is radius of the non-released part of either the transverse arms or the longitudinal stem, C_m is cupric ions concentration in r_1, and C_{m1} is cupric ions concentration in r_0.

When cupric ions release was in pseudo-steady state and under a perfect sink condition, the relationship between r_1 and the immersed time t of the nanocomposite IUD in media can be described by the following equation that is similar to Eq. (22) in literature [18].

$$\frac{r_1}{2}\ln\frac{r_1}{r_0}+\frac{1}{4}\left(r_0^2-r_1^2\right)+\frac{D_m h_s}{2KD_s r_0}\left(r_0^2-r_1^2\right)=\frac{D_m C_m}{A}t \qquad (1)$$

Where D_m is diffusion coefficient of the released cupric ions in matrix, D_s is diffusion coefficient of the released cupric ions in ambient media, h_s is thickness of the diffusion layer, K is distribution coefficient, and A is total content of the copper particles in nanocomposite IUD.

Apparently, for a given matrix-type solid drugs delivery system and a given immersed media, such as the nanocomposite IUD immersed in diluted nitric acid solution or SUS, all of r_0, D_m, D_s, h_s, K, C_m and A are constant, i.e., both $(D_m h_s/2KD_s)$ and $(D_m C_m/A)$ in Eq. (1) are constant. If $X=(D_m h_s/2KD_s+0.25)$ and $Y=(D_m C_m/A)$, then Eq. (1) can be replaced by Eq. (2).

$$\frac{r_1}{2}\ln\frac{r_1}{r_0}+X\left(r_0^2-r_1^2\right)=Yt \qquad (2)$$

That is to say, the cupric ions release mode of the novel γ-shaped Cu/LDPE nanocomposite IUD in SUS can be described with the formula that was given in Eq. (2).

3.4 Cupric ions release of the nanocomposite IUD in various volume of SUS

Influence of the immersion volume of SUS on the cupric ions concentration released by the γ-shaped nanocomposite

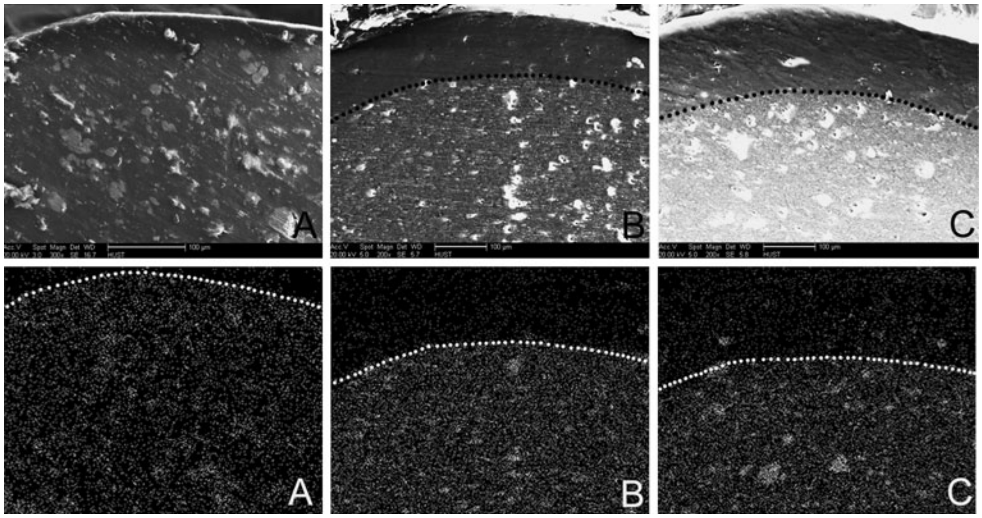

Fig. 5 SEM images and whole area copper profiles of the cross-section of the novel γ-shaped Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles after immersed in diluted nitric acid solution for **a** 0 day **b** 120 days, and **c** 240 days, respectively

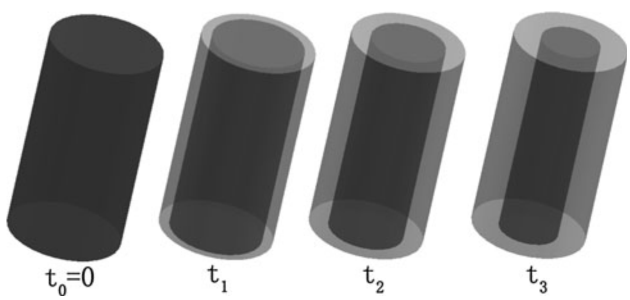

Fig. 6 Schematic illustration of the thickness of copper particles exhausted layer changes with the increasing of the immersion duration ($t_0 < t_1 < t_2 < t_3$)

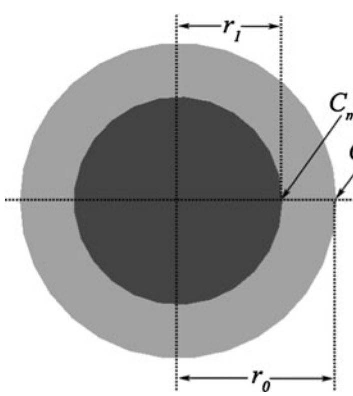

Fig. 7 Mathematical modeling of cupric ions release from the novel γ-shaped Cu/LDPE nanocomposite IUD (r_0 represent radius of either the transverse arms or the longitudinal stem, r_1 represent radius of the non-released part of either the transverse arms or the longitudinal stem, C_m represent cupric ions concentration in r_1, and C_{m1} represent cupric ions concentration in r_0, respectively)

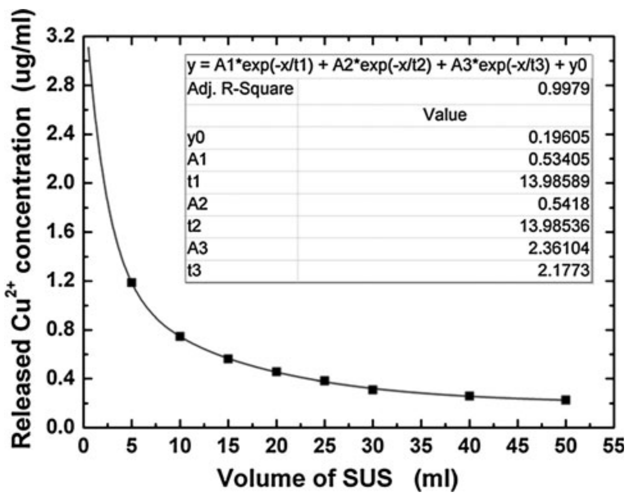

Fig. 8 Relationship between the cupric ions concentration released by the novel γ-shaped Cu/LDPE nanocomposite IUD with 25.0 wt% of copper nanoparticles and the immersion volume of SUS

IUD with 25.0 wt% of copper nanoparticles was given in Fig. 8. It can be seen that the immersion volume of SUS has remarkable influence on the released cupric ions concentration, and the released cupric ions concentration increase with the decreasing of immersion volume of SUS, indicating that an increase of the liquid volume will promote drug release due to lower drug concentration in the medium for a given volume of the drug controlled release system [25]. The fitting non-linear curve and its related equation were also given in Fig. 8, it can be seen that the fitting degree of the fitting curve is very well, and the cupric ions concentration released by the nanocomposite IUD in a certain volume of SUS can be obtained by using the equation shown in Fig. 8.

Similar to the existing Cu-IUD, the novel nanocomposite IUD need the same minimal cupric ions concentration to ensure its contraceptive efficacy. Many researches [26, 27] report that average cupric ions release rate of the existing Cu-IUD is from 7.3 to 84 μg/day. Although the mean endometrial volume of non-pregnant women is 5.8 ± 3.4 ml [28, 29], the volume of the uterine fluid is less than 1.0 ml [20, 21]. That is to say, even if half of the released cupric ions were absorbed by endometrium [30], the cupric ions concentration released by the existing Cu-IUD in uterine fluid is ranged from 3.65 to 42 μg/ml, it is apparently much larger than the minimal cupric ions concentration that need to ensure contraceptive efficacy. Recently, work of Bastidas show that the sperm motility almost decrease to zero at a cupric ions concentration of $\sim 8 \times 10^{-6}$ mol/l ($\sim$0.5 μg/ml) for a period of $\sim$20 min [17]. Indicating that 1.0 μg/ml of the cupric ions concentration is enough to inhibit the motility of human sperm in SUS even if half of the released cupric ions were absorbed by endometrium in vivo. Therefore, 1.0 μg/ml can be considered as the minimal cupric ions concentration that needs to ensure contraceptive efficacy of the nanocomposite IUD in clinical use.

From the equation shown in Fig. 8, it can be obtained that the cupric ions concentration released by the experimental nanocomposite IUD in 50 ml of SUS is about 11.9 times smaller than that in 1.0 ml of SUS. Indicating that, to ensure contraceptive efficacy of the novel nanocomposite IUD in the future clinical use, its released cupric ions concentration in 50 ml of SUS should be no less than 0.084 μg/ml. Here the cupric ions concentration was measured after the sample has been immersed in SUS for 24 h, thus the minimal cupric ions release rate in 50 ml of SUS that need to ensure contraceptive efficacy of the novel nanocomposite IUD in the future clinical use should be more than 4.2 μg/day.

In addition, it can be obtained from this experiment that the average cupric ions concentration released by the nanocomposite IUD with 25 wt% of copper particles in 50 ml of SUS is about 0.3822 μg/ml within 60 days and 0.3778 μg/ml within 120 days, i.e., its average cupric ions release rate in 50 ml of SUS is 19.11 μg/day within 60 days and 18.89 μg/day within 120 days.

3.5 Prospective life-span of the nanocomposite IUD

Apparently, no matter how much the copper nanoparticles content and the diameter is, all the cylindrical matrix-type nanocomposite IUD obey the same cupric ions release model as shown in Eq. (2). Therefore, prospective life-span of the cylindrical matrix-type nanocomposite IUD with certain concentration of copper particles can be obtained similarly: firstly, obtaining the relationship between the released cupric ions concentration and the immersion volume of SUS by experiment, and then obtaining the minimal cupric ions release rate in 50 ml of SUS that need to ensure its contraceptive efficacy in clinical use; secondly, obtaining the average cupric ions release rate of the nanocomposite IUD in 50 ml of SUS within two different immersion durations by the same experiment, and then converting the average cupric ions release rate within relevant immersion duration into its corresponding radius of the non-released part; thirdly, using these data to Eq. (2) and the constants X and Y can be obtained; finally, resolving the following equations and the prospective life-span (T) of the cylindrical matrix-type nanocomposite IUD with a diameter of r_0 can be obtained.

$$\frac{r_T}{2}\ln\frac{r_T}{r_0} + X \times \left(r_0^2 - r_T^2\right) = Y \times T \tag{3}$$

$$\frac{r_{T-1}}{2}\ln\frac{r_{T-1}}{r_0} + X \times \left(r_0^2 - r_{T-1}^2\right) = Y \times (T-1) \tag{4}$$

$$\frac{r_{T-1}^2 - r_T^2}{r_0^2} \times Z \times W \times 1000 = V \tag{5}$$

where X and Y are constants, r_T and r_{T-1} represent the radius of the non-released part of the cylindrical matrix-type nanocomposite IUD with Z wt% of copper particles after immersed in 50 ml of SUS for days of T and T-1, respectively; W (mg) is total weight of the cylindrical matrix-type nanocomposite IUD, and V (μg/day) is the minimal cupric ions release rate of the same nanocomposite IUD in 50 ml of SUS that need to ensure its contraceptive efficacy in clinical use.

Thus the prospective life-span (T) of the cylindrical matrix-type nanocomposite IUD with various contents of copper nanoparticles and various diameters in the future clinical use can be obtained in short-term.

For instance, the prospective life-span of γ-shaped nanocomposite IUD with 25 wt% of copper particles can be obtained as follows.

From the results of cupric ions release of the nanocomposite IUD in various volumes of SUS, it can be obtained that the average cupric ions release rate of the γ-shaped nanocomposite IUD with 25 wt% of copper particles in 50 ml of SUS is about 19.11 μg/day within 60 days and 18.89 μg/day within 120 days. The corresponding radius of the non-released part can be calculated easily and they are 0.991921 mm within 60 days and 0.983964 mm within 120 days, respectively. Using these data and r_0 of the present experimental nanocomposite IUD (i.e., 1.00 mm) in Eq. (2), the cupric ions release mathematical model of the novel nanocomposite IUD with 25

Table 1 Immersion duration (T) and corresponding radius (r_T) of the non-released part of the novel γ-shaped nanocomposite IUD with 25 wt% of copper particles when its cupric ions release rate is no less than 4.2 μg/day

Items	r_t (MM)	r_{T-1} (mm)	T (days)
Values	0.873900000	0.873933726	1827

wt% of copper particles in SUS can be obtained as the following equation described.

$$\frac{r_1}{2}\ln r_1 + 0.250666 \times \left(1 - r_1^2\right) = 1.794948 \times 10^{-7} \times t \quad (6)$$

In Eq. (6), if $t = T$ and T is the time that cupric ions release rate reduces to 4.2 μg/day in 50 ml of SUS, i.e., T is prospective life-span of the experimental nanocomposite IUD with a total weight of 285 mg, then the following equations can be obtained.

$$\frac{r_T}{2}\ln r_T + 0.250666 \times \left(1 - r_T^2\right) = 1.794948 \times 10^{-7} \times T \quad (7)$$

$$\frac{r_{T-1}}{2}\ln r_{T-1} + 0.250666 \times \left(1 - r_{T-1}^2\right) = 1.794948 \times 10^{-7} \times (T-1) \quad (8)$$

$$\left(r_{T-1}^2 - r_T^2\right) \times 25\% \times 285 \times 1000 = 4.2 \quad (9)$$

where r_T is radius of the non-released part of either the transverse arms or the longitudinal stem of the nanocomposite IUD with 25 wt% of copper particles after immersed in 50 ml of SUS for days of T, and r_{T-1} is radius of the non-released part of the same nanocomposite IUD after immersed in 50 ml of SUS for days of $T-1$.

From Eqs. (7–9), r_T, r_{T-1} and T can be obtained and they were tabulated in Table 1. It can be seen that the prospective life-span of the novel γ-shaped nanocomposite IUD with 25 wt% of copper particles is about 1827 days, i.e., 5 years in the future clinical use.

4 Conclusions

An approach is report to give prospective life-span of the novel γ-shaped Cu/LDPE nanocomposite IUD in the present work. It can be seen than the type of cupric ions release model of the novel γ-shaped nanocomposite IUD can be determined and verified by using approach of accelerated cupric ions release in diluted nitric acid solution in short-term, its cupric ions release behavior obeys the rule of solid drugs released from the cylindrical matrix-type drug delivery system very well. It also can be seen that the minimal cupric ions release rate for the nanocomposite IUD in 50 ml of SUS to ensure its contraceptive efficacy can be obtained by using the test of the cupric ions concentration release from the nanocomposite IUD in various volumes of SUS. Combining the corresponding radius of the non-released part that were obtained from its average cupric ions release rate in 50 ml of SUS within two different immersion durations, the prospective life-span of nanocomposite IUD can be predicted. For example, the prospective life-span of the novel γ-shaped nanocomposite IUD with 25 wt% of copper nanoparticles and 2 mm of diameter and a total weight of 285 mg is about 5 years in the future clinical application.

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