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Gold as a Biomedical Material

An international program to develop new uses for gold is producing results in the biomedical sector.

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Gold's beauty, permanence, and rarity mean that it has been revered by almost every culture and civilization throughout history. No substance has been more sought after than this rare metal, which has been a source of wealth, and which has been fabricated into religious artifacts, decorative articles, and jewelry, Fig. 1.

However, gold also demonstrates unique chemical and physical properties, and the gold mining industry has recently begun funding an international program to develop and promote gold in new industrial and medical applications. Currently, industrial applications (mainly in the electronics and dental sectors) amount to only around 12% of total gold demand, a conspicuously low figure compared to the other precious metals such as platinum.

This article describes the properties of gold that make it suitable for applications in the body, and describes past, present, and future medical applications of gold.

History of gold's medical benefits

Claims regarding the medical benefits of gold date back thousands of years. Ancient cultures in India and Egypt prepared gold-based medicines. In China, gold powders were used in the treatment of ailments such as smallpox and measles, while in Japan, tradition suggests that thin gold foils placed into drinks or food are beneficial to health.

Archaeological discoveries indicate that gold served in dental repairs as far back as the seventh century B.C. The Etruscans held substitute teeth in place with gold wire when their own were damaged, Fig. 2. The advantages of gold and its alloys for dental applications are related to its high biocompatibility, malleability, and resistance to corrosion. A typical crown and bridge alloy may contain 60 to 75% gold, with silver, platinum, and palladium added to make at least 75% noble metals, plus copper and zinc.

Gold and gold compounds have also historically been a component of drugs for the treatment of a wide range of ailments (chrysotherapy), including rheumatoid arthritis. In the last few decades, the properties of gold compounds have been of interest as potential cancer treatments. Researchers at the National University of Singapore have recently patented novel gold complexes in pharmaceuticals for the treatment of cancer, after they discovered that phosphine-supported gold complexes have excellent anti-tumor activity.

Fig. 1— Ancient gold jewelry. Image courtesy World Gold Council.

Medical devices

Today, a number of medical devices include at least some components of gold. As with dental applications, these are often related to the excellent biocompatibility of gold as a material. Stents for arteries have been plated with gold because it is highly opaque to X-rays, which aids in positioning of the stent. For a similar reason, doctors in Australia are testing gold in the treatment of prostate cancer. Small chips approximately the size of a grain of rice are inserted into the prostate with an ultrasound probe, a week or two before treatment. When patients undergo radiotherapy, doctors can accurately track where the prostate is on every day of the seven-week treatment, allowing the radiation to be more accurately targeted.

New research/feasibility studies

Supported by the world's leading gold mining companies, World Gold Council's *GROW* program (Gold *R*esearch *O*pportunities *W*orldwide) is currently supporting new research projects and feasibility studies at leading research centers around the world, with the aim of uncovering applications based on catalysis, nanotechnology, and electronics. One area that has already produced some exciting results is gold-based biomedical materials.

A feasibility study carried out at the Research Institute for Precious Metals (FEM) in Germany has been looking at the production of myringotomy tubes by electroforming gold. These tubes are implanted in the ear's tympanic membrane to drain and temporarily aerate the tympanic cavity. The barbell-shaped tubes are usually produced mechanically from silicone, gilded silver, or stainless steel. Gold, known for its excellent corrosion resistance, tissue biocompatibility, and high resistance to bacterial growth, represents an attractive material for the manufacture of these implants. Simultaneous electroforming of multiple tubes could significantly reduce the costs associated with the current mechanical preparation techniques.

Electroforming has traditionally been the method for production of hollow jewelry, dental restorations, and microelectromechanical systems (MEMS). In the current project, to fabricate electroformed gold tubes of the preferred shape, a three-stage production process was developed.

- First, a negative template of the multiple implants was produced by drilling holes with countersinks in an insulated aluminum sheet.
- Second, the implants were electroformed from gold, around the aluminum template.
- Third, the negative aluminum template was dissolved away by a sodium hydroxide solution, leaving the gold implants unaffected, Fig. 3.

In comparison with the current commercial tubes, the hardness values of the electroformed gold tubes were found to be quite low. However, this is not necessarily a disadvantage, as the only mechanical load the tubes have to withstand are related to insertion into the ear.

For other applications, tailoring of the properties may be required; for example, hardness could be increased through the addition of grain refiners. From the results

Fig. 2 — The ancient Etruscans used gold for dental repairs.

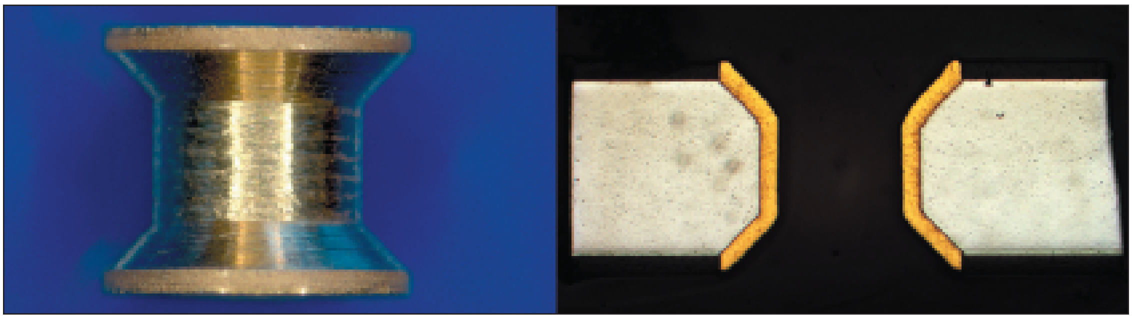

Fig. 3—Final electroformed gold tube, left, and cross-section of gold tube before aluminum template removal, right. Images courtesy FEM, Germany.

found during the project, it has been concluded that electroforming of gold can be easily adopted for the manufacture of medical implants. The simultaneous production of several implants offers the potential for substantial cost savings over traditional production methods.

Mesoporous gold

Another project funded through World Gold Council's *GROW* program has been potential applications for mesoporous gold sponges. Most highly porous or finely divided forms of metallic elements are pyrophoric, meaning that they are highly flammable. This is especially intense when the metal is porous at the nanoscale. Gold is a rare exception to this rule, and it has recently been shown by researchers at Mintek in South Africa that atmospherically stable, mesoporous sponges of gold can be prepared by controlled de-alloying of an intermetallic precursor, Fig. 4.

Researchers at Australia's University of Technology Sydney have been investigating whether mesoporous gold can function as an *in vivo* electrode, since it can both conduct electricity and serve as a storage reservoir for biologically active molecules. Mesoporous gold in this context is motivated by the observation that it is suitable to form an electrically conductive, porous scaffold on which to assemble functionalized coatings. Gold surfaces are very appropriate for such 'self-assembly,' because of their great nobility and affinity for sulfur. This allows functionalization with thiols or other organic molecules, modified to contain a sulfur atom. Such coatings with a high specific surface area could therefore act as highly sensitive biosensors.

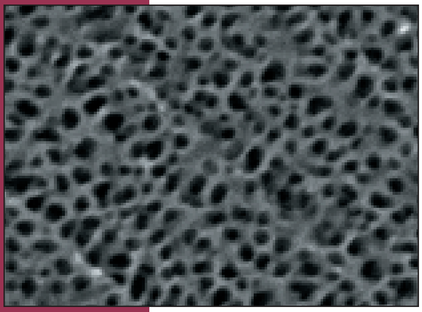

Fig. 4 — Mesoporous gold is a potential biomedical material. Image courtesy Mintek, South Africa.

Gold nanoparticles

In many instances, the potential application of gold in medicine is related to its interesting optical properties at the nanoscale.

• **Gold conjugate:** One example concerns the gold conjugate used in rapid tests. These tests are disposable membrane-based assays which, through visual evidence, indicate the presence of an analyte (chemical compound) in a liquid sample. Applications for rapid tests include clinical (such as pregnancy testing kits), agricultural, and environmental tests. The majority of available tests today are based on the unique properties of gold particles to develop the visual signal that confirms the presence of the analyte in the test fluid (urine, saliva, or blood). When applied to the device, the analyte in the sample (if present), attaches to the gold nanoparticles. This produces a distinct visual signal on the test device in the form of a sharp red line, which is the color characteristic of 40-nm gold nanoparticles. If the analyte is not present, then the gold nanoparticles are not observed, and the result is considered 'negative.'

• **Gold nanoshells**: In other biomedical applications, it is necessary to accurately target cells and tissue for localized heating or imaging. Human blood and tissue minimally absorb certain near-infrared wavelengths of light, enabling an external laser to deliver light to nanoshells either in a tumor (for thermal destruction or imaging) or a wound (for wound closure or tissue repair).

Gold nanoshells are a new type of optically tunable nanoparticle composed of a dielectric core such as silica, coated with a thin gold layer. Gold nanoshells can be made either to absorb or to scatter light preferentially by varying the size of the particle relative to the wavelength of the light at their optical resonance. This ability to tailor nanoshells to a specific wavelength is critical to such applications. Commercialization of this type of technology is now being pursued by companies such as Nano-spectra Biosciences Inc., Houston, Texas.

Work is continuing to develop these and similar concepts, but it is already clear that the role is growing for gold as a biomedical material. A subsequent article in *Advanced Materials and Processes* will describe developing applications for gold in other areas related to nanotechnology, including electronics and catalysis. **MPMD**

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