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Review article

# Coating Indwelling Urinary Catheter with Antibiotics Reduces Catheter-Associated Urinary Tract Infections

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**ABSTRACT**

Catheter-associated urinary tract infections (CAUTIs) are a common and significant healthcare-associated infection and represent the serious complicating bacterial infectious diseases. In the present review, the role of coating indwelling catheters with antibiotics in reducing the complicating bacterial infection, especially in critical urinary tract infections. There different urinary catheters are used to help patients that suffering from defects in the urination process. Different antibiotics were used in coating the indwelling urinary catheter (IUC) such as Gentamicin, Fluoroquinolones (Nitrofurazone, Norfloxacin, Ciprofloxacin, Sparfloxacin), and Triclosan. The effectiveness of coating IUC with antibiotics was dependent on the patient's clinical cases, the type of IUC, and the kind of antibiotic that would be used in the coating procedure. There are many restrictions in using the antibiotic coating IUC such as the producing the resistance strains and producing the allergy in patients. That is why, it is suggested to use antibiotic coating IUC is limiting in the serious CAUTIs.

**Keywords:** Antibiotics**,** Biofilm, CAUTIs, Coated Indwelling Urinary Catheter.

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## 1. INTRODUCTION

An ideal coating agent should be readily and inexpensively conjugated to the surface of the catheter while also having strong anti-biofilm/antimicrobial effectiveness [1]. Additionally, it must be biocompatible and avoid aggravating patient pain [2]. Catheter-associated urinary tract infections (CAUTIs) are a common and significant healthcare-associated infection. They occur when bacteria or other microorganisms enter the urinary tract through the urinary catheter, which is a tube inserted into the bladder to drain urine in patients who are unable to urinate normally. To address the problem of CAUTIs, researchers have explored various strategies, including coating urinary catheters with antibiotics. The idea behind antibiotic-coated catheters is to provide a localized antimicrobial effect directly at the catheter's surface, preventing bacterial colonization and reducing the risk of infection [3]. The antibiotics used in catheter coatings typically belong to the class of broad-spectrum antimicrobial agents [4]. These antibiotics have activity against a wide range of bacteria, including both Gram-positive and Gram-negative bacteria commonly associated with CAUTIs such as *Escherichia coli, Pseudomonas aeruginosa*, and *Staphylococcus aureus* [5]. The concept of antibiotic-coated catheters gained attention due to the potential benefits they offer in reducing CAUTIs. The antimicrobial properties of the coating help inhibit bacterial growth and prevent the formation of biofilms on the catheter's surface, which are known to be key factor in the development of CAUTIs. However, it is important to note that the effectiveness of antibiotic-coated catheters in reducing CAUTIs has been a subject of debate and further investigation. Factors such as the specific type of coating, patient population, duration of catheterization, and compliance with infection prevention protocols can influence the outcomes [6]. Additionally, concerns about antibiotic resistance and potential adverse effects associated with the use of antibiotic-coated catheters have also been raised. Prolonged exposure to low levels of antibiotics may contribute to

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the emergence of resistant bacterial strains, limiting treatment options for infections [6]. It is important to weigh the potential benefits against the risks and consider the judicious use of antibiotic-coated catheters in appropriate patient populations. In recent years, healthcare guidelines and recommendations have suggested that the use of antibiotic-coated catheters should be reserved for specific high-risk patient populations or cases where alternative prevention strategies have failed [7]. As research and understanding in this area continue to evolve, healthcare providers need to stay updated on the latest evidence and guidelines to make informed decisions regarding the use of antibiotic-coated urinary catheters

## 2. URINARY CATHETER

It is a plastic flexible tube implanted into the bladder to drain urine. It is used in special clinical cases when a patient is unable to urinate on their own or when it is necessary to accurately measure urine output. Catheterization may be required in various medical situations, including during surgery, for individuals who are immobilized or critically ill, and for people with urinary retention or incontinence [8]. There are different types of urinary catheters available, including an indwelling catheter (Foley catheter), it is a common type of catheter that remains in the bladder for an extended period. It has a small balloon at the end that is inflated with sterile water to keep the catheter in place [9]. The other end of the catheter is connected to a drainage bag that collects urine. The intermittent catheter is the second type of catheter that is inserted into the bladder to drain urine and then removed. It is typically used for short-term catheterization and can be done by the individual or with the assistance of a healthcare professional. Another type of urinary catheter is a suprapubic catheter which is inserted directly into the bladder through a small incision made in the lower abdomen. It is often used when long-term catheterization is necessary or when the urethra cannot be used for catheter insertion. Urinary catheterization should be performed by an expert healthcare professional to minimize clinical mistakes such as infection and injury [10].

The use of urinary catheters can be traced back thousands of years. The earliest known use of catheters dates back to ancient times. Ancient Egyptians, Greeks, and Romans were known to use various materials like reeds, metal tubes, and hollowed-out plant stems to create primitive catheters for draining the bladder. In the 16$^{th}$ Century, the Renaissance period, advancements were made in the design and materials used for catheters. French physician Ambroise Paré introduced the idea of using a silver tube as a catheter. The use of silver was believed to have antibacterial properties. In the 17$^{th}$ and 18$^{th}$ centuries, further improvements were made in catheter design and materials. The French surgeon Pierre Dionis developed a flexible catheter made of goose quills, which was an improvement over the rigid metal tubes used previously. In the 19$^{th}$ century, rubber catheters were introduced, which provided increased flexibility and comfort for patients. The invention of vulcanization by Charles Goodyear in the 1830s allowed for the mass production of rubber catheters. In the 20$^{th}$ century, advancements in medical technology and materials led to the development of disposable catheters, reducing the risk of infection and improving patient comfort. Catheters made from plastics, such as polyvinyl chloride (PVC), became more widely used. In recent decades, further advancements have been made in catheter technology [11]. This includes the development of specialized catheters for different purposes, such as Foley catheters with inflatable balloons, and antimicrobial-coated catheters to reduce the risk of infection.

## 3. URINARY CATHETER MATERIALS

Standard urinary catheters have been made from a variety of materials, including silicone, latex, plastic, siliconized latex, silicone elastomers, polytetrafluoroethylene (PTFE), hydrogel-coated latex, and latex coated with both hydrogel and hydrophilic polymers [12]. The patient needs to get a test to select the best materials made from the catheter for use before implementing it in his/her body. Due to their better non-allergenic and flow characteristics, as well as their resistance to kinking, silicone catheters are also favored over latex ones [13]. For patients who experience frequent blockage, the Centers for Disease Control and Prevention (CDC) advises silicone catheters over those made of other materials [13]. To lessen urethral microtrauma, the CDC also advises patients who need intermittent catheterization to utilize hydrophilic catheters rather than conventional catheters. Urinary bacteria can still colonize the catheter and cause infections despite the range of materials. Urinary catheter materials have been altered by the addition of anti-fouling or bactericidal coatings to inhibit bacteria colonization and biofilm development [4].

## 4. CATHETER COATING MATERIALS

There are different materials used in coating urinary catheters depending on the specific type and purpose of the catheter. It's important to note that not all urinary catheters have coatings. Some catheters may have a smooth, uncoated surface. The choice of coating depends on factors such as the intended use, patient needs, and manufacturer specifications. It's always advisable to consult with a healthcare professional or read the manufacturer's instructions for specific information on the materials and coatings used in a particular urinary catheter. There are some common materials used for coating urinary catheters:

*Hydrophilic Coating*: Modern urinary catheters are characterized by a hydrophilic coating, which becomes slippery when in contact with water or body fluids. This coating reduces roughness during insertion and withdrawal, making the catheterization process more comfortable for the patient. Hydrophilic coatings are typically made from materials such as polyvinylpyrrolidone (PVP) or hydrophilic polymers [4].

*Silicone Coating:* Silicone coatings are used in some urinary catheters to improve biocompatibility and reduce friction. Silicone is a smooth and flexible material that can enhance patient comfort during catheterization [4].

*Lubricious Coating*: They are applied to urinary catheters to reduce friction during insertion and withdrawal. These coatings can be made from various materials, such as hydrogels or silicone-based lubricants.

*Antimicrobial Coating*: Some urinary catheters may have an antimicrobial coating to help reduce the risk of urinary tract infections (UTIs). These coatings often contain antimicrobial agents such as silver, nitrofurazone, or chlorhexidine. The antimicrobial agents are released gradually from the coating, helping to inhibit the growth of bacteria on the catheter's surface [4].

### 4.1. Antibiotics coating IUC

The most important strategy followed by doctors in the treatment of infectious diseases caused by bacteria is the use of antibiotics to fight bacterial infections, especially those responsible for catheter-associated urinary tract infections (CAUTIs). For decades, many researchers have used antibiotics for coating the IUC to reduce urinary tract infections associated with catheterization, but their effectiveness was variable. The current study reviews the most important antibiotics used in urinary catheter encapsulation and the effectiveness of these antibiotics [14].

### 4.1.1. Gentamicin

Gentamicin is a broad-spectrum antibiotic that belongs to the aminoglycoside class of antibiotics. It is commonly used to treat various bacterial infections, including urinary tract infections (UTIs) caused by susceptible bacteria. Gentamicin works by inhibiting bacterial protein synthesis, thereby preventing the bacteria from growing and multiplying [15]. It is effective against many gram-negative bacteria, as well as some gram-positive bacteria. The first use of this antibiotic was in coating the IUC catheter that was used in the animal model to reduce CAUT. The results were highly encouraging for the scientist to be used in further clinical experiments. Another study showed that the addition of polyethylenecovinyl acetate (PEG) to gentamicin was effective in controlling the release of the antibiotic for up to 12 days [16].

### 4.1.2. Fluoroquinolones

Fluoroquinolones are a class of antibiotics that are commonly used to treat a variety of bacterial infections. They are characterized by their chemical structure, which includes a fluorine atom. Fluoroquinolones work by inhibiting the activity of enzymes called DNA gyrase and topoisomerase IV, which are essential for bacterial DNA replication and repair. By interfering with these enzymes, fluoroquinolones prevent the bacteria from multiplying and spreading. The examples of fluoroquinolones that were used in coating the IUC are nitrofurazone, Norfloxacin, Ciprofloxacin, and Sparfloxacin [4].

### 4.1.3. Nitrofurazone

Nitrofurazone is an antimicrobial agent that belongs to the nitrofuran class of drugs. It is used as a topical treatment for various skin infections and wounds. Nitrofurazone works by inhibiting the growth and multiplication of bacteria by inhibiting DNA replication [3]. Nitrofurazone has broad-spectrum activity against many Gram-positive and Gram-negative bacteria (*Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus,* and vancomycin-resistant *Enterococcus faecium* [4]. Moreover, this type of antibiotic is highly effective against fungi thus, it is traditionally used to treat skin infections. The coating IUC with nitrofurazone yielded mixed results in clinical settings. The previous study showed no decrease in the incidence of CAUTI. On the other hand, the experiments of clinical trials showed a decrease in symptomatic CAUTI when nitrofurazone catheters were used in place of Teflon-coated latex catheters with a borderline significant drop in CAUTI frequency [17]. The study by Zhu et al. (2019) showed no uncomfortable for patients who used the nitrofurazone catheters [3].

### 4.1.4. Norfloxacin

Norfloxacin is a fluoroquinolone antibiotic used to treat various bacterial infections. It is a broad-spectrum antibiotic that inhibits the growth and multiplication of susceptible bacteria (*E. coli, K. pneumoniae, P. vulgaris, and P. aeruginosa*) [18]. Norfloxacin shows efficacy when combined with other antibiotics against biofilm formation *in vitro*. It is commonly prescribed for the treatment of urinary tract infections (UTIs), including uncomplicated UTIs caused by susceptible bacteria. It may also be used for other types of infections, such as prostatitis, gastrointestinal infections, and certain sexually transmitted infections. Norfloxacin works by interfering with bacterial DNA synthesis, specifically targeting the enzymes DNA gyrase and topoisomerase IV. By inhibiting these enzymes, norfloxacin disrupts bacterial DNA replication and repair, ultimately leading to bacterial cell death. This study also concluded that at this concentration, bactericidal activity was effective as early as 24 h [19]. The effectiveness of norfloxacin-coated catheters in vivo and during clinical trials, however, has not been assessed.

### 4.1.5. Ciprofloxacin

Ciprofloxacin is a fluoroquinolone antibiotic used to treat a wide range of bacterial infections. It is a broad-spectrum antibiotic effective against both gram-negative and gram-positive bacteria such as *E. coli, K. pneumoniae, Pseudomonas aeruginosa*, *S. aureus,* and *Proteus mirabilis.* Ciprofloxacin is commonly prescribed for various infections, including urinary tract infections (UTIs), respiratory tract infections, skin and soft tissue infections, bone and joint infections, gastrointestinal infections, and certain sexually transmitted infections. It is also sometimes used to prevent or treat infections in people with weakened immune systems. It works by inhibiting the activity of bacterial enzymes called DNA gyrase and topoisomerase IV. These enzymes are essential for bacterial DNA replication and repair. By interfering with these enzymes, ciprofloxacin prevents bacteria from multiplying and causes them to die off. The previous study by Pugach et al (1999) used the ciprofloxacin liposomes-impregnated hydrogel Foley catheters and they found that the *E. coli* CAUTI was delayed 3.5 days as compared with uncoated catheter [4].

### 4.1.6. Sparfloxacin

It was primarily used for the treatment of bacterial infections, particularly respiratory tract infections such as bronchitis and pneumonia and *E. coli* and *S. aureus* CAUTI [20]. Sparfloxacin works by inhibiting the bacterial enzymes necessary for DNA replication and transcription, thus preventing the growth and reproduction of the bacteria causing the infection. It has a broad spectrum of activity against both Gram-positive and Gram-negative bacteria. Kowalczuk et al (2012) used sparfloxacin-coated catheters in their study [20].

### 4.1.7. Triclosan

It inhibits the enzymatic activity responsible for fatty acid synthesis [21]. Triclosan is a synthetic antimicrobial agent that has been widely used in personal care products, such as soaps, hand sanitizers, toothpaste, and cosmetics. It has also been used in other products like clothing, kitchen utensils, and furniture. Triclosan works by inhibiting the growth of bacteria and some fungi. Several studies have suggested that triclosan may contribute to antibiotic resistance by promoting the development of resistant strains of bacteria [4]. Recently, triclosan has been proposed as a candidate for coating medical devices, since its chemical properties make it easy to coat the catheter material [4].

## 4.2. Restriction of using antibiotic-coated IUC.

Continuous exposure to low levels of antibiotics from the catheter coating may contribute to the emergence of antibiotic-resistant bacteria. This can have implications not only for the individual patient but also for public health, as resistant bacteria can spread to others and limit treatment options. Another concern is the potential for allergic reactions or adverse effects associated with the antibiotic coating itself. Some individuals may be hypersensitive or allergic to the specific antibiotics used in the coating, which can lead to complications. Due to these concerns, regulatory authorities and professional organizations have recommended caution or limitations on the use of antibiotic-coated urinary catheters. For example, the Centers for Disease Control and Prevention (CDC) in the United States suggests that antibiotic-coated catheters should be reserved for specific patient populations who are at high risk for CAUTIs and have limited treatment options [3].

Because some antibiotics such as nitrofurazone have been demonstrated to be carcinogenic, the U.S. Food and Drug Administration (FDA) stopped approving it as a topical antiseptic for use on humans and food animals in May 2002. Catheters are not covered by this change since this prohibition only applies to topical nitrofurazone purchased over the counter. As a result, they are still used in clinics, although nitrofurazone research and interest have declined [3, 22]. Due to these worries, regulatory bodies including the European Chemicals Agency (ECHA) and the U.S. Food and Drug Administration (FDA) have taken steps to restrict or outright forbid the use of several antibiotics in coating urinary catheters such as triclosan.

## 5. CONCLUSION

The current study has shown that coating the urine catheter with certain types of antibiotics, especially broad-spectrum antibiotics, contributes in most cases to reducing CAUTIs. However, the efficiency of coated with antibiotics depends on the type of antibody as well as the patient's health condition. In general, it is recommended that allergy tests be conducted before using these types of catheters. Even if they do not cause allergic reactions in the patient, they are recommended for use in patients with critical conditions.

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**Conflict of interest**

The authors declare that they have no conflict of interests.

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