Alcaligenes Faecalis, An Opportunistic Pathogen of Multidrug Resistance

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Abstract

Alcaligenes faecalis, naturally found in soil and water is also found to be present as a member of normal human microbiota. Some of the strains are found to cause diseases of human, both adult and new-born, some of which are life threatening. *A faecalis* strains are also found to cause diseases in birds like poultry birds and turkeys; some vertebrates and nematodes. The most dangerous fact is that most of these strains are resistant to almost all existing antibiotics and this resistance is conferred by antibiotic resistant genes (ARG), constituting the resistomes. Being a free-living organism, under the stress of environment and antimicrobials present therein, *A faecalis* finds shelter in living body. In course of time, it turns to opportunistic pathogen in the immune compromised hosts and as result of rampant use of antibiotics for both empiric and definitive therapy of the diseases, few strains become multi drug resistant. The biofilm mediated infections conferred by these antibiotic resistant strains give rise to various chronic and nosocomial diseases in human.

Key words: *Alcaligenes faecalis*; antibiotic; multi-drug resistance; microbiota; nosocomial diseases.

1. Introduction

The large diversity of microbiota in soil has a significant impact on the ecosystem. *Alcaligenes faecalis* is a common free-living bacterium found in soil and water that is generally considered nonpathogenic. However, over time, it developed a preference for the internal environment of the human body and was first isolated from human faeces. This shift in habitat could be the result of accidental entry into the human body as a contaminant in food and drink. The evolution of a parasitic lifestyle from a free-living lifestyle includes the acquisition of new functions required to survive on or within the host, transmit between hosts, and exploit the host's resources (Poulin et al, 2015)

As an opportunistic pathogen, *A. faecalis* acquires the ability to withstand antibiotic stress and develops resistance to a variety of antibiotics. It eventually becomes a parasite of humans and other animals, causing a variety of diseases. Because of increased resistance to several antibiotics, *Alcaligenes faecalis* infection is frequently difficult to treat, and many strains become pan drug resistant. The current review focuses on the pathogenic properties of this bacterium in humans and nonhuman animals.

2. Diseases caused by *A faecalis*:

In healthy people, infections do not occur. Many infections are caused by medical device contamination. Clinical infections in humans with compromised and uncompromised immune systems (Fig 1) have been linked to opportunistic infections (Pathogen Safety Data Sheet, 2017). Most common method of communication is faecal oral route; contaminated medical equipment. As nosocomial infections, immunocompromised hospitalized patients may contract the infection from ventilators, intravenous solutions, and hemodialysis systems.

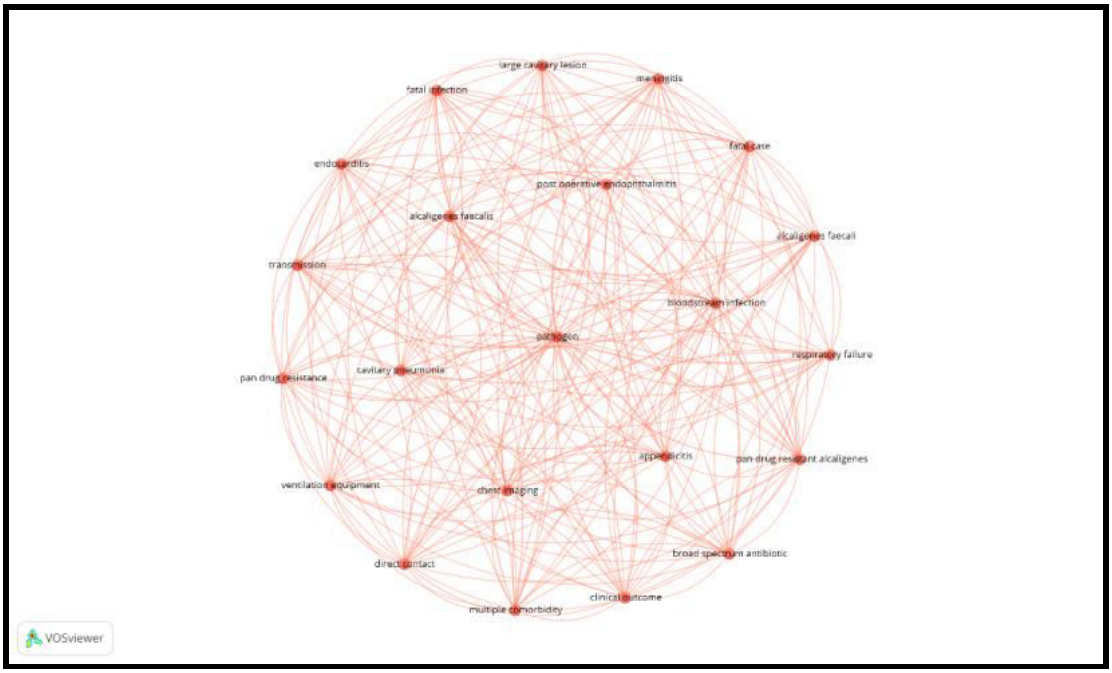

Fig 1. VOS viewer bibliometric analysis of diseases caused by *Alcaligenes faecalis*

2.1. Diseases in human

Alcaligenes faecalis is a free-living aerobic bacterium that is found in the environment and often acts as a heterotrophic nitrifier. Because E. faecalis exists as a symbiont in the human alimentary canal, infections are not found in healthy humans. Many infections in post-operative patients are caused by contaminated medical devices. After surgical removal of the appendix, a case of *Alcaligenes faecalis* septicemia was reported (Skegg, 1976). After six months of mechanical aortic valve replacement, some abnormal activity was detected near the site of prosthetic valve implantation.

The involvement of *Alcaligenes faecalis* was revealed by repeated peripheral blood cultures (Vogiatzis, and Koutsampasopoulos, 2019). However, few early reports on its pathogenicity were available following its discovery in faeces (Table 1).

A. *faecalis* is the most common inhabitant of human gut associated lymphoid tissues (Shimoyama, et al. 2021)and is considered a representative of human symbiont bacteria because *A. faecalis* DOS7 was isolated from human faeces (Loiko et al, 2022). It has been linked to a number of biofilm-mediated chronic diseases, including bacteremia, endocarditis,

Table 1. Early reports of human disease causing *Alcaligenes faecalis*

Reported Disease	**References**
Meningitis	Terry, *et al* .1947
Meningitis, Conjunctivitis, Rheumatic fever, Hepatitis	Weinstein, and Wasserman, 1951
Acute meningitis	Peluffo,1951
meningitis and bacteremia	Wynne *et al, 1952*
Suppurative meningitis	Bauza *et al*, 1952
Septicemia	Dureux, *et al*.1953
Septicaemia	Librach. 1954
Septicaemia in new-born	Doxiadis, *et al*. 1960
Measles encephalitis	Mengedoht, *et al*. 1960
Infection of new-born	Sherman, et al 1960
Septicaemia in new-born	Khetarpal, 1964
Septicaemia and meningitis in new born	Berry, 1967
Septicemia	Desai, *et al.* 1983
Septicemia and meningitis in new born	Kishan., *et al*. 1987

endophthalmitis, meningitis, cellulitis, urinary tract infections, otitis media, peritonitis, and pneumonia. It has been discovered to be the causative agent of postoperative endophthalmitis in humans. In humans, *A. faecalis* frequently causes Urinary Tract Infection (UTI), which can be fatal. Because the urinary tract is one of the most common sites of *A faecalis* infection, bacteria can enter the urine through the urethra, travel to the bladder, and even reach the kidney. Women are more prone to UTI than men due to shorter urethras, which bacteria must travel through to reach the bladder. They are also found in GALT in Peyer's patch, where they maintain a balance with the internal environment of the dendritic cells by lowering the rate of programmed cell death and increasing the rate of mitochondrial respiration (Hosomi, et al, 2020).

It was reported that *A faecalis* caused an unusual skin and soft tissue infection (Tena, et al 2015). The most common symptoms were vascular ulcerative infection and infection at the surgical site. Based on these symptoms, *A. faecalis* is a potential pathogen of skin and soft tissue infection, especially after surgery or in patients with vascular diseases. Antibiotic resistance makes treatment more difficult.

Eight patients with diabetic foot ulcers (Huang, 2020a) were reported which were caused by *A. faecalis* infection, five of whom were males and three of whom were females.

This pathogen is responsible for a number of uncommon deadly infections, including appendicitis, abscesses, meningitis, bloodstream infection, endocarditis, and post-operative endophthalmitis (Al-Zakhari, et al 2020). It was discovered that there is an emerging trend for multidrug resistance against all commercially available antibiotics, and that this trend is spreading globally. According to recent researchers (Hasan, et al. 2019), nosocomial infections caused by *A. faecalis* are common in hospitalized patients. Although serious lethal infections are uncommon, several case studies demonstrate their harmful nature. This bacterium was found to be the cause of a rare case of meningitis in an immunocompromised patient (Cantillo et al 2022).

Scientists (Huang, 2020a) conducted a six-year retrospective study on 61 adults infected with A faecalis. The majority of patients had cystitis, followed by diabetic foot ulcers, acute pyelonephritis, and pneumonia, and a few had bacteremia and infection at specific sites. Bacterial infections can occur with *E. faecalis* infections, and the most commonly associated bacteria are *Enterococcus species*, *Proteus vulgaris*, and

Pseudomonas aeruginosa. Despite their presence, *A faecalis* is considered to be the major pathogen that should be treated with special care due to antibiotic resistance.

The most common order of *A faecalis* infection targets were the blood vessels followed by urinary tract, skin and soft tissue, and middle ear. It was observed that with adequate intravenous antibiotic therapy, patients with *A faecalis* infection will typically experience a positive treatment outcome.

A thirty-year-old man with no noteworthy co-morbidities complained of epigastric/chest discomfort, nausea, and vomiting for a few days (Bhagia, et al 2022) He was slightly tachycardic, tachypneic, and appeared dehydrated with flushed skin, according to medical examinations. According to haematological reports, RBC and WBC counts were normal, with elevated platelets and elevated ESR and C-reactive protein. Although the initial electrocardiogram (ECG) and echocardiogram results were normal, a CT scan of the abdomen/pelvis revealed bilateral adrenal hemorrhage. However, blood cultures revealed the presence of *A faecalis*, which is susceptible to cephalosporins. However, the patient recovered after receiving proper antibiotics targeting *A faecalis* and having his adrenal insufficiency treated with steroid therapy.

2.1.1. Case studies:

First testified instance of *A. faecalis* infection was found from the bronchoalveolar washing of a patient, suffering from dengue hemorrhagic fever (Agarwal, et al 2017).

Chest imaging revealed a large cavitary lung lesion in a sixty-six-year-old male patient suffering from respiratory failure and other comorbidities (Al-Zakhari et al, 2020) and was found to be caused by the multidrug-resistant *A. faecalis*. Despite being treated with broad-spectrum antibiotics, his rate of recovery was woefully inadequate. As a result, they concluded that *A. faecalis,* despite being a natural inhabitant of the intestine, can cause serious illnesses and even death.

In another case, a sixty-year-old woman with high blood sugar and high blood pressure, was admitted to a hospital's intensive care unit with a high fever, altered state of consciousness, and lower abdominal pain. She was diagnosed with a bloodstream infection caused by *A. faecalis*(Hasan, et al. 2019). The pathogen could not be killed by any commercially available antibiotics, including carbapenems, tigecycline, and polymyxins, resulting in the patient's health rapidly deteriorating. However, doubling the dose of tigecycline might have eliminated the disease (Hasan, et al. 2019).

Another study was conducted in Angola (Filipe, et al 2017). on approximately one hundred patients with chronic diseases like suppurative otitis media (CSOM). They investigated the antibiotic sensitivity of *A faecalis* strains found in patients' ear discharge fluid. These bacterial strains were discovered to be fluoroquinolone antibiotic resistant (100% resistant to Ciprofloxacin and 82.6% resistant to levofloxacin).

A case of *A. faecalis* mediated osteomyelitis of the right lower extremity was discovered in a patient with a long-lasting diabetic foot ulcer (Smith, et al 2022).

A survey was conducted in the department of Internal Medicine, Taiwan (Huang, 2020b). on all *A. faecalis*-infected patients admitted to Dalin Tzu Chi Hospital between January 2014 and December 2019. Data from the hospital's record of medical, clinical, and microbiological reports revealed that sixty-one patients had *A. faecalis* infection. Only twenty-five of them had UTIs, nine had diabetic foot ulcers, mine had skin problems, eight had pneumonia, nine had infections at various sites, seven had acute pyelonephritis, and three had bacteremia. It was discovered that more than half of these patients received intravenous antibiotic treatment, indicating the presence of antibiotic resistance in the bacteria. It was also discovered that antibiotics like ciprofloxacin (fluoroquinolone antibiotic), piperacillin/tazobactam (a combination of piperacillin and the β-lactamase inhibitor), amikacin (aminoglycoside antibiotic), and cefepime (a fourth-generation cephalosporin) are not good choices for empiric therapy of *A. faecalis* infection.

A very rare case of bloodstream infection caused by a strain of *A. faecalis* that was resistant to all existing antibiotics was described (Hasan, et al. 2019), but could be successfully treated with a double-dose of tigecycline.

A patient got post-operative endophthalmitis as a result of an *A faecalis* infection (Srinivasan, et al 2008). *A. faecalis*, which is frequently present in the human digestive tract as normal microbiota, occasionally causes disease, usually in immunocompromised hosts, but also in patients with biofilm-mediated diseases such as

acute otitis media, peritonitis, and eye or urinary tract infections. The bacteria are commonly found in avian stool and can frequently cause opportunistic infections (Filipe, et al 2017).To date, no outbreaks of *A. faecalis* pseudo bacteraemia have been reported. But such pseudo-bacteraemia has caused an *A. faecalis* epidemic in neonatology and pediatric units. As a result, rather than being regarded as a mere contaminant, it should be regarded as a serious pathogen capable of causing life-threatening infections. Furthermore, the emergence of pan-drug-resistant strains of *A. faecalis* has become a major global concern.
Between 2003 and 2008, 72 strains of *A. faecalis* were isolated from various clinical samples for antibiotic sensitivity testing. 30%, 19.6%, and 14% of these strains were isolated from surgical patients, outpatient clinic patients, and Dermatology Department patients, respectively. A large number of strains were isolated from infected material samples, whereas only 16.7% of strains could be isolated from urine samples. All of the strains tested positive for antibiotics such as piperacyline, piperacyline/tazobactam, and carbapenems. About half of the strains were resistant to co-trimoxazole, and 80% were resistant to aztreonam(Jachna-Sawicka and Gospodarek, 2009). Most of the diseases reported (Table 2) are biofilm mediated and hence were difficult to treat by antibiotics.

2.2. *Alcaligenes faecalis* infection in the newborn

Although *A. faecalis* is not considered a pathogen for newborns, it caused meningitis in a nine-day-old premature twin who recovered after being treated with chloramphenicol. Three children were reported to have diarrhea and bloody stools, one of which was fatal. There were three reports of new-born

Table.2: Various Case reports indicating the pathogenic attributes of *Alcaligenes faecalis*

Source of sample	Disease	Reference
Respiratory tract	Cavitary pneumonia	Al-Zakhari, et al 2020.
Respiratory tissue	cystic fibrosis (CF),	Dunne, et al, 1995
Respiratory tissue	cystic fibrosis (CF),	Liu *et al* 2002.
Respiratory tissue	meningitis in new born	Knippschill, *et al* 1996
Pancreas	pancreatic abscess	Ashwath, et al, 2005
Cornea	corneal ulcer	Hwang, *et al* 2009
Blood	bacteremia and respiratory infections	Manfredi, *et al*, 1997
Wound sample	Wound Sepsis	Mordi *et al* 2013
Blood	Candidemia associated infections	Siddiqui, *et al*. 2015
Ear discharge	acute otitis	Bizet and Bizet ,1997
Urine	urinary tract infection and diarrhoea.	Bizet and Bizet ,1997
Foot pus.	perforating ulcers of the left foot	Bizet and Bizet ,1997
Urine.	paraplegia and neurological bladder.	Bizet and Bizet ,1997
Urine	pelvic malformation.	Bizet and Bizet ,1997
Tibial pus	femur fracture.	Bizet and Bizet ,1997
Urine of an ICU patient	Reported antibiotic resistance	Pereira *et al*. 2000
Ophthalmic fluid	Post keratoplasty endophthalmitis	Khokhar *et al*. 2002
Blood	hematologic malignancies, neutropenia Diabetes mellitus	Aisenberg *et al*. 2004
Urine	Nosocomial infections	Dubois, *et al*, 2006
Ophthalmic condition	Postoperative endophthalmitis	Kaliaperumal*et al*. 2006
Peritoneal fluid	peritonitis	Kavuncuoglu et al, 2010
Peritoneal fluid	peritonitis	Kahveci, et al. 2011
Ocular fluid	Endophthalmitis after cataract surgery	Pal, et al, 2013
Sample from vascular ulcer infection and surgical spot infection.	Skin and soft tissue infection (SSTI)	Tena, et al 2015

CSF	Cerebrovascular complications of meningitis	Prasad, et al,2016
Ear discharge	Chronic Suppurative Otitis Media hearing loss	Filipe, et al 2017
Wound culture	cellulitis secondary to a dog bite,	Chu et al, 2017
Bronchoalveolar fluid	bronchopneumonia	Agarwal, et al 2017
Sputum sample	Pneumonia and hemodynamically unstable.	Junejo, et al, 2018.
Blood samples	Infective endocarditis with skin lesions.	Vogiatzis, &Koutsampasopoulos,, 2019
Blood samples	bloodstream infection	Hasan, *et al*. 2019
	increase in inflammatory parameters	Majewski *et al* 2020

fatal meningitis, two of which were associated with bacteraemia. A 2-week-old infant was also reported to have bilateral conjunctivitis(Sherman, et al 1960).

A newborn was found with unusual manifestations of septicemia and meningitis caused by *A faecalis* infection (Berry ,1967). There have been 130 reported cases of *A faecalis* infection, the majority of which involved newborns and infants. Four such cited case reports were available (Khetarpal, 1964). the first of which described a boy of a twin who died after seven days of birth from raspatory problems that could not be cured by terramycin treatment. *A faecalis* was detected in the blood culture. Another prematurely delivered baby died as a result of jaundice. Despite receiving corticosteroids and Achromycin at the same time, the baby died. Another baby admitted with jaundice had *A faecalis* in his blood. He recovered after receiving terramycin treatment. Tetracycline also cured another newborn with jaundice that had *A faecalis* in his blood. These reports clearly show *A faecalis* infection in newborns and a proclivity for antibiotic resistance.

2.3. *Alcaligenes faecalis* infection in animals

A faecalis is most commonly found in chickens, turkeys, and other birds (Pathogen Safety Data Sheet, Nipissing University ,2017).Scientists isolated*A faecalis* strains from apparently healthy turkeys (Varley 1986) and discovered that UK isolates showing rhinotracheitis were less pathogenic than foreign isolates. Some of the isolates isolated from tracheal swabs caused severe respiratory disease and death in turkey poults. This bacterium has also been linked to chicken disease (Montgomery, et al. 1983).*A. faecalis*-associated respiratory disease was discovered not only in chickens but also has been identified as the primary pathogen responsible for *Alcaligenes rhinotracheitis*, a respiratory disease in domestic turkeys (Simmons, et al. 1981).

Respiratory infections in chicks are usually severe and often fatal, but optimal antibiotic therapy to combat them is not well established (Osawe, F. O., & Osagie2012), (Mordi, et al2013). *A. faecalis* is commonly found in bird faeces and can cause opportunistic infections in these animals (Gerlach. et al,1994) . A 19-month-old boy is presented with cellulitis caused by a dog bite that did not respond to oral antibiotic therapy and progressed to worsening fever and swelling. *A. faecalis* grew in the wound culture, and its identity was confirmed using recombinant DNA (Chu, and Harkness, 2017).

A. faecalis ANSA176 was isolated from donkey intestinal chyme and found to have a high OTA-detoxifying ability (Zheng, 2022).. The bacterium could also be isolated from the large marine fish *Argyrosomus regius*(Gutiérrez-Falcón, *et al.* 2021).

It was discovered to be a normal resident of 39 (65%) of the 60 dogs' conjunctival sacs (Sarchahi, et al 2005). Mastitis is caused by the bacterium attacking the udder of cattle (Bacterial Diseases of Cattle, ,2007). Some invertebrates have been found to harbour*E. faecalis*. It is found as a symbiotic bacterial species in the EPN *Oscheius* spp., an entomopathogenic nematode (Shan, et al 2019).The bacteria were discovered in the oesophagus and intestines of the nematodes *Steinernemafeltiae, S. carpocapsae, and H. bacteriophora*(Quiroz-Castañeda, et al (2015).

3. Antibiotic resistance of *Alcaligenes faecalis*

Most strains appeared to have multiple antibiotic resistance, including -lactams (amoxicillin, ticarcillin, and aztreonam), aminoglycosides, and quinolones, but were susceptible to combinations of amoxicillin or ticarcillin plus clavulanic acid and cephalosporins (Pathogen Safety Data Sheet, 2017).

In 1997,*A. faecalis* strains were first reported to be resistant to antibiotics such as amoxicillin, ticarcillin, and gentamicin, and that such resistance could be passed down through chromosomal gene mutations and horizontal gene transfer(Bizet and Bizet 1997). The bacteria have been found to be resistant to β-lactam, fluoroquinolone, and aminoglycoside antibiotics, and this resistance is attributed to various antibiotic breaking enzymes encoded by specific genes (Lang, *et al.* 2022).

Dubois reported the existence of an A. faecalis strain with extended-spectrum β-lactamases (ESBL) from a patient with a concurrent urinary tract infection (Dubois, *et al*, 2006).

A patient with dengue hemorrhagic fever infected with a strain of A faecalis with high antibiotic resistance was discovered(Agarwal, et al 2017).

A. faecalis strain (MUB14) was isolated from a myeloid leukemia patient who was admitted to the hospital with a high fever. A significant increase in inflammatory parameters was observed on Day 15 of hospitalization, and a pan drug resistant A. faecalis MUB14 was isolated from the patient's urine Majewski P, *et al* (2020).

Fifteen strains of *A. faecalis* from various clinical samples were isolated that were resistant to antibiotics such as imipenem, meropenem, amikacin, gentamicin, tobramycin, ciprofloxacin, levofloxacin, ticarcillin, tigecycline, trimethoprim/sulbactam, piperacillin/tazobactam, cefoperazoneKhajuria, *et al*. (2013).

A faecalis isolate from a lung lesion in a 66-year-old respiratory patient demonstrated resistance to sulfamethoxazole/trimethoprim, tobramycin, tazobactam/piperacillin, and gentamicin, as well as levofloxacin and ciprofloxacin (Al-Zakhari, et al 2020).

A strain of *A. faecalis* causing chronic suppurative otitis media was discovered from Angola, which is resistant to fluoroquinolone, a highly effective broad spectrum antibiotic (Wisplinghoff, 2017).

The urinary tract infection-causing strain of *A faecalis*, on the other hand, was found to be removed by a therapeutic dose of norfloxacin (Ju, *et al* ,2016), a quinolone antibiotic [400 mg twice daily for 10 days], or cotrimoxazole, a trimethoprim-sulfamethoxazole [160/800 mg twice daily for 10 days] .

An alarming trend of increasing resistance to various antibiotics was demonstrated in 2020 (Huang, 2020b)., including Amikacin, Ceftazidime, Cefepime, Ampicillin-sulbactam, Gentamicin, Piperacillin-tazobactam, Ciprofloxacin, Imipenem, Meropenem, and Tygacil (from 2014 to 2019). Many pan drug resistant A faecalis strains have been discovered in countries such as India, Bangladesh, and Palestine(Tena, , et al 2015)

The full list of antibiotics used in *A. faecalis* susceptibility testing, including piperacillin, piperacillin-tazobactam, ceftazidime, cefepime, cefotaxime, ceftriaxone, ampicillin-sulbactam, imipenem, meropenem, gentamicin, amikacin, ciprofloxacin, levofloxacin, levof(Wisplinghoff, 2917)

The resistome of *A faecalis* has been discovered to contain various antibiotic resistant genes (ARGs), based on which the strains are classified into four groups, namely

Cluster I: Strain AN70, Cluster II: Strain AN70, Cluster III: Strain AN70, Cluster IV: Strain AN70, Cluster V: Strain AN

Cluster II: Strains (P156, ZD02, PGB1, DSM30030, and FDAARGOS 491), Cluster III: Strains (P156, ZD02, PGB1, DSM30030, and FDAARGOS 491) (BDB4, AU14, and MC250)

Group IV: Strains (JQ135, J481, and QD168)

PGB1 Alcaligenes faecalis was isolated and found to be resistant to penicillin and three other antibiotics. ARGs are primarily responsible for antibiotic efflux and -lactamase production (Lang, *et al.* 2022)

The most dangerous aspect of an *A. faecalis* infection is its resistance to almost all common antibiotics. As a pan drug resistant antibiotic, it has 50% sensitivity to ciprofloxacin and piperacillin and 66.7% sensitivity to carbapenem antibiotics. Experiments with A faecalis isolates treated with antibiotics revealed that antibiotics such as aminoglycoside amikacin, cephalosporins, and colistin can kill almost 100% of the

bacteria, whereas gentamicin, tobramycin, and piperacillin/tazobactam can kill 90% of the bacteria, and trimethoprim/sulfamethoxazole can kill 75%.

Most isolates, on the other hand, were resistant to antimicrobials such as fluoroquinolones ciprofloxacin and levofloxacin. It has been discovered that there is a rapid increase in antimicrobial resistance in *A. faecalis* to commonly used antibiotics. Patients in various cases reported extreme antibiotic resistance. The antibiotic susceptibility testing (Huang, 2020b). with the VITEK® II system and VITEK® II Gram Negative Susceptibility cards (bioMérieux, Marcy-l'Étoile, France) using Clinical & Laboratory Standards Institute interpretive criteria M100-25. Resistome analysis in *A. faecalis* ZD02 was performed to examine the bacteria's resistance to various antibiotics. (Lang, *et al.* 2022)

4. Probable cause of contradictory attributes of *A faecalis*.

A. faecalis, which is commonly found in the natural environment, is thought to survive by effectively adapting with its surroundings. As pollution has increased, they have evolved the excellent ability to degrade a wide range of contaminants, from heavy metals to plastic and other hydrocarbons (Ju, *et al*. 2016). and this has made them a promising candidate for the bioremediation of environmental pollution(Bharali *et al*. 2011). In order to strive other competitors in the plant rhizosphere they have developed pesticidal activities. On the other hand, some of them took up the parasitic life, mainly within mammalian and avian hosts (Fig 2).

However, the dual quality of *A faecalis* cannot be explained solely by the "avirulence hypothesis" or the "trade-off hypothesis" (Brown, *et al* 2012). Antibiotic resistance genes in *A faecalis* strains that attack the body as a pathogen are activated by the vast and diverse types of antibiotics currently used to treat infections. On the contrary, open-environment strains are less antibiotic resistant than clinical strains.

Changes in natural ecosystems, such as the release of large amounts of antimicrobials, may alter the population dynamics of microorganisms, including resistance selection, with uncertain consequences for human health (Martinez, 2009).

The selective pressures of the environment, whether abiotic or biotic, most likely pave the way for 'coincidental evolution of virulence' (Alizon, and Michalakis, 2015). This has been exacerbated by the gradual accumulation of antibiotic resistance genes (Diard and Hardt , 2017).

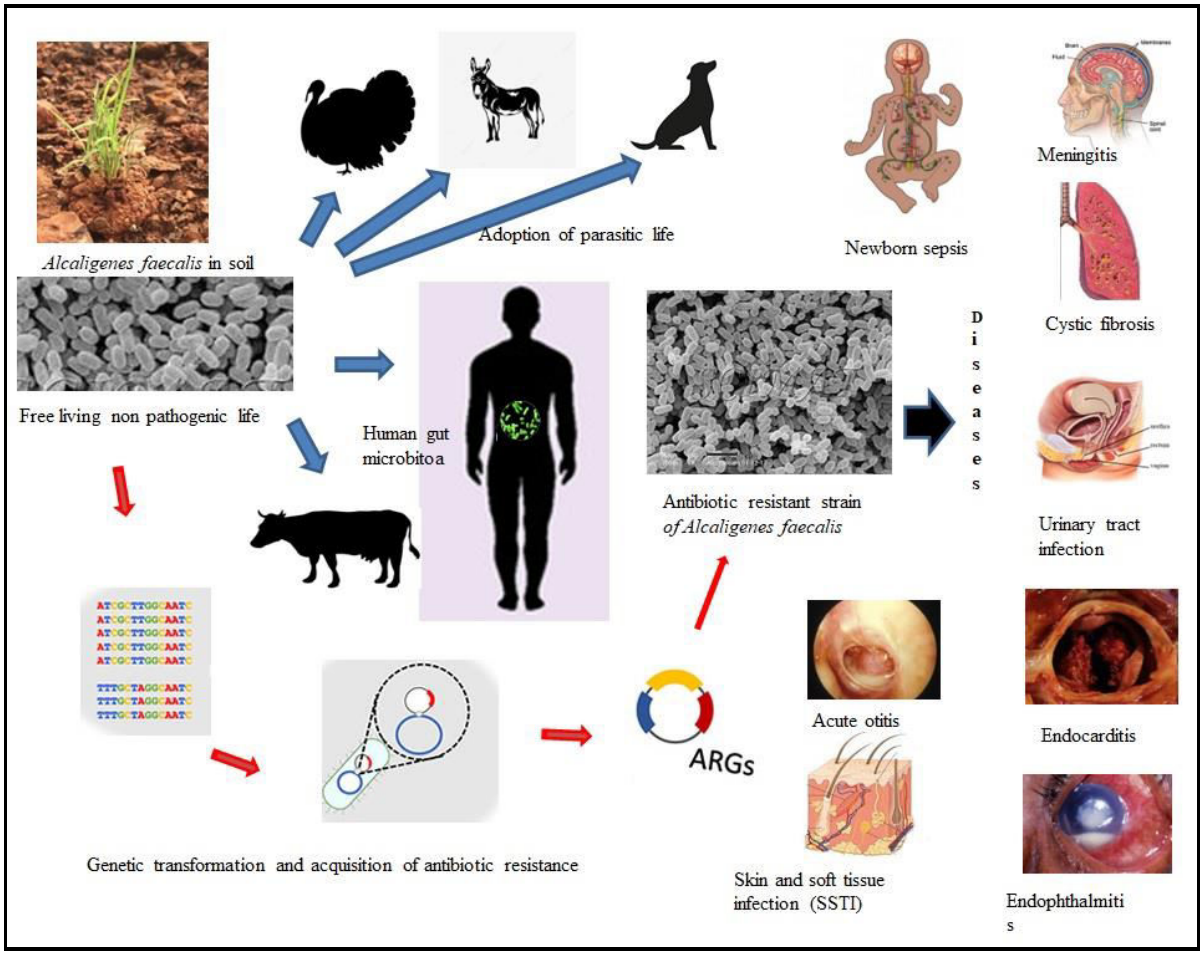

Fig 2. Transformation of lifestyle of *Alcaligenes faecalis* from free living, soil dwelling to parasitic (human and some other mammals and birds) and pathogenic form

Conclusion

A faecalis strains can be found in soil, water, and the atmosphere, as well as the human body, and are usually non-pathogenic. However, opportunistic infections can have serious, even fatal, consequences. These infections are mostly caused by nosocomial infections and are exacerbated by antibiotic resistance. On the one hand, these bacteria are capable of bioremediation, but they also cause serious biofilm-mediated diseases. These activities have made the bacteria important in terms of both the environment and medicine.

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Reference

1. Agarwal, A., Sharma, S., Bhargava, V., Bhargava, V., Agarwal, M., & Airun, M. (2017). First reported case of Alcaligenes faecalis isolated from bronchoalveolar lavage in a patient with dengue hemorrhagic fever. *J Assoc Chest Physicians*, *5*(1), 51-5.
2. Aisenberg, G., Rolston, K. V., & Safdar, A. (2004). Bacteremia caused by Achromobacter and Alcaligenes species in 46 patients with cancer (1989–2003). *Cancer*, *101*(9), 2134-2140.
3. Alizon, S., & Michalakis, Y. (2015). Adaptive virulence evolution: the good old fitness-based approach. *Trends in ecology & evolution*, *30*(5), 248-254.

4. Al-Zakhari, R., Suhail, M., Ataallah, B., Aljammali, S., &Grigos, A. (2020). Rare but fatal case of cavitary pneumonia caused by Alcaligenes faecalis. *Cureus*, *12*(6).
5. Ashwath, M. L., & Katner, H. P. (2005). Pancreatic abscess secondary to Alcaligenes faecalis. *The American journal of the medical sciences*, *329*(1), 54-55.
6. Bacterial Diseases of Cattle, Molecular Diagnostic Services, Inc., San Diego, CA 92121,2007.
7. Bauza, C. A., Amarante, A., & Prunell, A. L. (1952). Meningitis purulentapor*Alkaligenes faecalis*en un lactante [Suppurative meningitis in infant caused by *Alcaligenes faecalis*]. *Archivos de pediatria del Uruguay*, *23*(8), 534–538.
8. Berry, A. M. (1967). B. alcaligenes faecalis septicemia and meningitis in the newborn: report of an unusual case. *The Indian Journal of Pediatrics*, *34*, 242-244.
9. Bhagia, G., Kumar, S., & Bansal, P. (2022). *Alcaligenes faecalis*: could it be any weirder than we thought? *Journal of the American College of Cardiology*, *79*(9_Supplement), 3446-3446.
10. Bharali, P., Das, S., Konwar, B. K., & Thakur, A. J. (2011). Crude biosurfactant from thermophilic Alcaligenes faecalis: Feasibility in petro-spill bioremediation. *International Biodeterioration & Biodegradation*, *65*(5), 682-690.
11. Bizet, J., & Bizet, C. (1997). Strains of Alcaligenes faecalis from clinical material. *Journal of Infection*, *35*(2), 167-169.
12. Brown, S. P., Cornforth, D. M., &Mideo, N. (2012). Evolution of virulence in opportunistic pathogens: generalism, plasticity, and control. *Trends in microbiology*, *20*(7), 336-342.
13. Cantillo García, K., Calderón Duran, O., Acosta Pérez, T., Vásquez Jiménez, Á., Madrid Pérez, E., Martínez-Ávila, M. C., ... & Almanza-Hurtado, A. (2022). A Rare Case of Meningitis Caused by Alcaligenes faecalis in an Immunocompetent Patient. *Case Reports in Medicine*, *2022*.
14. Chu, A. S., & Harkness, J. (2017). Alcaligenes faecalis cellulitis after a dog bite: case report and literature review. *Pediatric Emergency Care*, *33*(7), 497-498.
15. Desai, N., Gupta, S.K., Menon, R.K. , Seth V. (1983). *Alcaligenes fecalis*scpticemia. *Indian J Pediat* **50**, 687–689
16. Diard, M., & Hardt, W. D. (2017). Evolution of bacterial virulence. *FEMS microbiology reviews*, *41*(5), 679-697.
17. Doxiadis, S. A., Pavlatou, M., &Chryssostomidou, O. (1960). Bacillus faecalis alcaligenes septicemia in the newborn. *The Journal of Pediatrics*, *56*(5), 648-654.
18. Dubois, V., Arpin, C., Coulange, L., Andre, C., Noury, P., & Quentin, C. (2006). TEM-21 extended-spectrum β-lactamase in a clinical isolate of Alcaligenes faecalis from a nursing home. *Journal of Antimicrobial Chemotherapy*, *57*(2), 368-369.
19. Dunne Jr, W. M., & Maisch, S. (1995). Epidemiological investigation of infections due to Alcaligenes species in children and patients with cystic fibrosis: use of repetitive-element-sequence polymerase chain reaction. *Clinical infectious diseases*, *20*(4), 836-841.
20. Dureux, J., De Lavergne, E., & Burdin, J. C. (1953). A propos d'un cas de septicémie à faecalis alcaligenes [A case of Alcaligenes faecalis septicemia]. *Revue medicale de Nancy*, *78*, 304–310.
21. Filipe, M., Reimer, Å., Matuschek, E., Paul, M., Pelkonen, T., & Riesbeck, K. (2017). Fluoroquinolone-resistant Alcaligenes faecalis related to chronic suppurative otitis media, Angola. *Emerging Infectious Diseases*, *23*(10), 1740–1742.
22. Gerlach H(1994) Bacteria in Avian medicine: principles and applications. Lake Worth (FL, USA): Wingers Publishing; p. 949–83 ISBN 0-9636996-0-1
23. Gutiérrez-Falcón, A. I., Ramos-Nuez, A. M., de los Monteros y Zayas, A. E., Castillo, D. P., García-Laorden, M. I., Chamizo-López, F. J., ... & Martín-Barrasa, J. L. (2021). Probiotic properties of Alcaligenes faecalis isolated from Argyrosomus regius in experimental peritonitis (rat model). *Probiotics and Antimicrobial Proteins*, *13*(5), 1326-1337.
24. Hasan, M. J., Nizhu, L. N., & Rabbani, R. (2019). Bloodstream infection with pandrug-resistant Alcaligenes faecalis treated with double-dose of tigecycline. *IDCases*, *18*, e00600.

25. Hosomi, K., Shibata, N., Shimoyama, A., Uto, T., Nagatake, T., Tojima, Y., ... &Kunisawa, J. (2020). Lymphoid Tissue–Resident Alcaligenes Establish an Intracellular Symbiotic Environment by Creating a Unique Energy Shift in Dendritic Cells. *Frontiers in Microbiology*, *11*, 561005.
26. Huang, C. (2020a). Diabetic foot ulcer with Alcaligenes faecalis infection. *Dubai Diabetes and Endocrinology Journal*, *26*(3), 128-133.
27. Huang, C. (2020b). Extensively drug-resistant Alcaligenes faecalis infection. *BMC Infectious Diseases*, *20*(1), 1-11.
28. Hwang, J. H., Kim, M. J., Kweon, E. Y., Ahn, M., & You, I. C. (2009). A Case of Corneal Ulcer by Alcaligenes Faecalis. *Journal of the Korean Ophthalmological Society*, *50*(9), 1414-1417.
29. Jachna-Sawicka, K., & Gospodarek, E. (2009). Udziałpałeczek Alcaligenes faecalis w zakazeniachpacjentówszpitalauniwersyteckiego w Bydgoszczy [Evaluation of occurrence of Alcaligenes faecalis in clinical samples of patients of the university hospital in Bydgoszcz]. *Medycynadoswiadczalnaimikrobiologia*, *61*(1), 87–92.
30. Ju, S., Lin, J., Zheng, J., Wang, S., Zhou, H., & Sun, M. (2016). Alcaligenes faecalis ZD02, a novel nematicidal bacterium with an extracellular serine protease virulence factor. *Applied and environmental microbiology*, *82*(7), 2112-2120.
31. Junejo, S. Z., Tuli, S., &Trandafirescu, T. (2018). A rare case of pneumonia caused by Alcaligenes faecalis bacteria. In *B52. Bacterial Infection Case Reports* (pp. A3602-A3602). American Thoracic Society.
32. Kahveci, A., Asicioglu, E., Tigen, E., Ari, E., Arikan, H., Odabasi, Z., &Ozener, C. (2011). Unusual causes of peritonitis in a peritoneal dialysis patient: Alcaligenes faecalis and Pantoeaagglomerans. *Annals of Clinical Microbiology and Antimicrobials*, *10*, 1-3.
33. Kaliaperumal, S., Srinivasan, R., Gupta, A., & Parija, S. C. (2006). Postoperative endophthalmitis due to an unusual pathogen: Alcaligenes faecalis. *Eye*, *20*(8), 968-969.
34. Kavuncuoglu, F., Unal, A., Oguzhan, N., Tokgoz, B., Oymak, O., & Utas, C. (2010). First reported case of Alcaligenes faecalis peritonitis. *Peritoneal Dialysis International*, *30*(1), 118-119.
35. Khajuria, A., Praharaj, A. K., Kumar, M., & Grover, N. (2013). Emergence of VIM-6 metallo-beta-lactamase-producing Alcaligenes faecalis clinical isolates in a hospital in India. *The Journal of Infection in Developing Countries*, *7*(06), 494-496.
36. Khetarpal, S. K. (1964). B. alcaligenes faecalis septicemia in the newborn. *Clinical Pediatrics*, *3*(2), 108-110.
37. Khokhar, D. S., Sethi, H. S., Kumar, H., Sudan, R., Sharma, N., & Nayak, N. (2002). Postkeratoplasty endophthalmitis by Alcaligenes faecalis: a case report. *Cornea*, *21*(2), 232-233.
38. Kishan, J., Elzouki, A. Y., & Mir, N. A. (1987). Bacillus Alcaligenes fecalissepticemia and meningitis in the newborn. *The Indian Journal of Pediatrics*, *54*(5), 789-790.
39. Knippschild, M., Schmid, E. N., Uppenkamp, M., König, E., Meusers, P., Brittinger, G., &Höffkes, H. G. (1996). Infection by Alcaligenes xylosoxidans subsp. xylosoxidans in neutropenic patients. *Oncology*, *53*(3), 258-262.
40. Lang, J., Li, Y., Yang, W., Dong, R., Liang, Y., Liu, J., ... & Meng, B. (2022). Genomic and resistome analysis of Alcaligenes faecalis strain PGB1 by Nanopore MinION and Illumina Technologies. *BMC genomics*, *23*(1), 1-15.
41. Librach, I. M. (1954). B. Faecalis Alkaligenes Infections with a Report of a Case of Septicaemia. *Postgraduate Medical Journal*, *30*(346), 424–429.
42. Liu, L., Coenye, T., Burns, J. L., Whitby, P. W., Stull, T. L., & LiPuma, J. J. (2002). Ribosomal DNA-directed PCR for identification of Achromobacter (Alcaligenes) xylosoxidans recovered from sputum samples from cystic fibrosis patients. *Journal of clinical microbiology*, *40*(4), 1210-1213.
43. Loiko, N., Kanunnikov, O., Gannesen, A., Kovalenko, V., Vishnyakova, A., Axelrod, V., &Litti, Y. (2022). Brain Natriuretic Peptide (BNP) Affects Growth and Stress Tolerance of Representatives of the Human Microbiome, Micrococcus luteus C01 and Alcaligenes faecalis DOS7. *Biology*, *11*(7), 984.

44. Majewski, P., Majewska, P., Gutowska, A., Piszcz, J., Sacha, P., Wieczorek, P., ... & Tryniszewska, E. (2020). Molecular characterisation of clinical pandrug-resistant Alcaligenes faecalis strain MUB14. *International journal of antimicrobial agents*, *55*(6), 105939.
45. Manfredi, R., Nanetti, A., Ferri, M., & Chiodo, F. (1997). Bacteremia and respiratory involvement by Alcaligenes xylosoxidans in patients infected with the human immunodeficiency virus. *European Journal of Clinical Microbiology and Infectious Diseases*, *16*, 933-938.
46. Martinez, J. L. (2009). Environmental pollution by antibiotics and by antibiotic resistance determinants. *Environmental pollution*, *157*(11), 2893-2902.
47. Mengedoht, M. M., Aton, J. K., & Berry, A. (1960). A case of measles encephalitis complicated by Alcaligenes faecalis septicemia. *The Journal of Pediatrics*, *57*(5), 738-740.
48. Montgomery, R. D., Kleven, S. H., & Villegas, P. (1983). Observations on the pathogenicity of Alcaligenes faecalis in chickens. *Avian Diseases*, 751-761.
49. Mordi, R. M., Yusuf, E. O., Onemu, S. O., Igeleke, C. L., &Odjadjare, E. E. (2013). The prevalence of Alcaligenes faecalis in bacteremia, meningitis and wound sepsis in a tertiary health care institutions in Western part of Nigeria. *Int. J. Biotechnol*, *2*(7), 123-129.
50. Osawe, F. O., & Osagie, A. O. (2012). Unusual cause of palatal ulcer in a parial denture wearer: Alcaligenes species. *Journal of Medicine and Biomedical Research*, *11*(2), 76-79.
51. Pal, S. S., Panigrahi, P. K., Roy, R., Nandi, K., & Das, S. (2013). Endophthalmitis caused by Alcaligenes faecalis: a case series. *Ocular Immunology and Inflammation*, *21*(6), 446-448.
52. Peluffo, E., Surraco, N. L. (1951). Meningitis agudaspor faecalis Alkaligenesenreciénnacidos [Acute meningitis due to Alcaligenes faecalis in newborn]. *Archivos de pediatria del Uruguay*, *22*(2), 105–107.
53. Pereira, M., Perilli, M., Mantengoli, E., Luzzaro, F., Toniolo, A., Rossolini, G. M., &Amicosante, G. (2000). PER-1 extended-spectrum β-lactamase production in an Alcaligenes faecalis clinical isolate resistant to expanded-spectrum cephalosporins and monobactams from a hospital in Northern Italy. *Microbial Drug Resistance*, *6*(1), 85-90.
54. Poulin, R., & Randhawa, H. S. (2015). Evolution of parasitism along convergent lines: from ecology to genomics. *Parasitology*, *142*(S1), S6-S15.
55. Prasad A, Anwer S, Martinez C (2016) Acute Embolic Infarcts from *Alcaligenes Faecalis* Meningitis: A Case Report. Journal of Neuroinfectious Diseases, 7:203.
56. Quiroz-Castañeda, R. E., Mendoza-Mejía, A., Obregón-Barboza, V., Martínez-Ocampo, F., Hernández-Mendoza, A., Martínez-Garduño, F., ... &Dantán-González, E. (2015). Identification of a new Alcaligenes faecalis strain MOR02 and assessment of its toxicity and pathogenicity to insects. *BioMed research international*, *2015*.
57. Sarchahi, A. A., Haghkhah, M., &Molazem, M. (2005). Antimicrobial susceptibility of canine normal conjunctival flora in Shiraz, Iran. *Vet Online: International Journal of Veterinary Medicine*, 1.(1), 1-6
58. Shan, S., Wang, W., Song, C., Wang, M., Sun, B., Li, Y., ... & Rasmann, S. (2019). The symbiotic bacteria Alcaligenes faecalis of the entomopathogenic nematodes Oscheius spp. exhibit potential biocontrol of plant-and entomopathogenic fungi. *Microbial Biotechnology*, *12*(3), 459-471.
59. Sherman, J. D., Ingall, D., Wiener, J., &Pryles, C. V. (1960). Alcaligenes faecalis infection in the newborn. *American Journal of Diseases of Children*, *100*(2), 212-216.
60. Shimoyama, A., Di Lorenzo, F., Yamaura, H., Mizote, K., Palmigiano, A., Pither, M. D., Speciale, I., Uto, T., Masui, S., Sturiale, L., Garozzo, D., Hosomi, K., Shibata, N., Kabayama, K., Fujimoto, Y., Silipo, A., Kunisawa, J., Kiyono, H., Molinaro, A., & Fukase, K. (2021). Lipopolysaccharide from Gut-Associated Lymphoid-Tissue-Resident Alcaligenes faecalis: Complete Structure Determination and Chemical Synthesis of Its Lipid A. *AngewandteChemie (International ed. in English)*, *60*(18), 10023–10031.

61. Siddiqui, N., Kirmani, S., Khan, F., Kaushal, N., Shukla, I. K., Khan, H. M., ... & Jahan, S. (2015). Prevalence and risk factors of Candida blood stream infections in a tertiary care hospital. *Int J CurrMicrobiol App Sci*, *1*, 157-62.
62. Simmons, D. G., Davis, D. E., Rose, L. P., Gray, J. G., & Luginbuhl, G. H. (1981). Alcaligenes faecalis-associated respiratory disease of chickens. *Avian diseases*, 610-613.
63. Skegg, D. C. (1976). Alcaligenes faecalis septicemia. *The New Zealand Medical Journal*, *83*(558), 117-119.
64. Smith, J. C., Comianos, M., Tang, W., & Sarvepalli, S. (2022). Right Lower Extremity Osteomyelitis With Alcaligenes faecalis in a Patient With Poorly Controlled Type 2 Diabetes Mellitus. *Cureus*, *14*(11).
65. Srinivasan, R., Gupta, A., Kaliaperumal, S., Babu, R. K., Thimmarayan, S. K., &Belgode, H. N. (2008). Efficacy of intraoperative vancomycin in irrigating solutions on aqueous contamination during phacoemulsification. *Indian journal of ophthalmology*, *56*(5), 399-402
66. Tena, D., Fernández, C., & Lago, M. R. (2015). Alcaligenes faecalis: an unusual cause of skin and soft tissue infection. *Japanese journal of infectious diseases*, *68*(2), 128-130.
67. Terry, L. L., McBane, J. K., & Dean, K. F. (1947). Bacteremia and Acute Meningitis due to Alcaligenes faecalis. A Case Report. *Journal of Laboratory and Clinical Medicine*, *32*(10), 1262-5.
68. Varley, J. (1986). The characterisation of Bordetella/Alcaligenes-like organisms and their effects on Turkey Poults and chicks. *Avian Pathology*, *15*(1), 1-22.
69. Vogiatzis, I., &Koutsampasopoulos, K. (2019). Infective endocarditis caused by Alcaligenes faecalis complicated with skin lesions. *Anatolian Journal of Cardiology*, *21*(5), E10.
70. Weinstein, L., & Wasserman, E. (1951). Bacterium alcaligines (Alcaligines faecalis) infections in man. *New England Journal of Medicine*, *244*(18), 662-665.
71. Wisplinghoff H. Infectious Diseases (Fourth Edition) Vol. 2. Amsterdam: Elsevier; 2017. Pseudomonas spp., Acinetobacter spp. and miscellaneous Gram-negative bacilli; pp. 1579–1599.
72. Wynne, E. S., Old, J. W., & Gott, C. L. (1952). Alcaligenes Faecalis Meningitis and Bacteremia Concurrent with Bacillary Dysentery. *American Journal of Clinical Pathology*, *22*(3), 267-270.
73. Zheng, R., Qing, H., Ma, Q., Huo, X., Huang, S., Zhao, L., Zhang, J & Ji, C. (2022). A Newly Isolated Alcaligenes faecalis ANSA176 with the Capability of Alleviating Immune Injury and Inflammation through Efficiently Degrading Ochratoxin A. *Toxins*, *14*(8), 569.