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Review Article

### Using of some plant extracts against multidrug resistant *klebsiella* species isolated from different sources

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#### Abstract

**K**lebsiella species specially *klebsiella pneumoniae* considered an important pathogenic bacteria affecting human causing (pneumonia, gastrointestinal problems), animal causing (mastitis, respiratory disorders and neonatal septicemia) and has a significant public health concern due to its presence in various food sources (raw, cooked, and processed meats, vegetables, fruits, milk and milk products) and its multiple resistance to different antimicrobial agents, these resistance cause a great threat world wide, because using of these different antibiotics become of no value and the side effect of these different drugs affect human and animal health. These bacteria become more virulent and resistant due to the biofilm formation which is the ability of microbe to protect itself from the surroundings and immune system of the host. therefore, searching for anew approach to overcome this problem become in concern, like medicinal plants and their extracts which used as antimicrobial agents against many animal and human pathogens like *klebsiella* species, the derived compounds from these plants has antimicrobial action evaluated through laboratory trials after isolation and identification of bacteria (*klebsiella* species), so that this review aimed to increased awareness and gather information about this micobe and its prevalence from different sources, resistance profiles, virulence factors and different plant extract used against *K. pneumoniae* to assess the risks to public health and made effective strategies to control its impact on consumers.

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## Introduction

*Klebsiella* spp is an important pathogen and Avery common member of the Enterobacteriaceae found in Intestinal tract of animals and man, soil, water, sewage, plants, other places in the environment as sawdust cause severe bacterial infections of the cardiovascular, respiratory, gastrointestinal, renal systems in humans and animals, *also* normally found in human stool (feces) that can cause healthcare-associated infections (HAIs). (Kowalczyk *et al.*, 2022; Wareth and Neubauer, 2021) and also are a common contaminant in many fresh foods such as meat, milk, fish, vegetables and products such as street food. Therefore, they were considered a significant foodborne pathogen (Davis and Price, 2016; Kakatkar *et al.*, 2017). *Klebsiella* are non motile, rod-shaped, gram-negative bacteria with a prominent polysaccharide capsule. This capsule encases the entire cell surface, accounts for the large appearance of the organism on gram stain, and provides resistance against many host defense mechanisms. *Klebsiella* species are serogrouped by 2 types of antigens on their cell surface. The first is a lipopolysaccharide (O antigen); the other is a capsular polysaccharide (K antigen). Both of these antigens contribute to pathogenicity. About 77 K antigens and 9 O antigens exist. The structural variability of these antigens forms the basis for classification into various serotypes. The virulence of all serotypes appears to be similar. *Klebsiella* have been described. K1, K2 and K5 are venereal transmitted and are the predominant types in the isolates from metritis in mares. (Markey *et al.* 2013). The genus *Klebsiella* has many species are associated with illness in humans and animals as *K. aerogenes*, previously known as *Enterobacter aerogenes* and *Bacterium aerogenes* *K. granulomatis*, *K. oxytoca*, *K. michiganensis*, *K. pneumoniae* (type-species) (*K.p.* subsp. *Ozaenae* *K. p.* subsp. *Pneumonia*, *K.p.* subsp. *Rhinoscleromatis*) *K. quasi pneumoniae* (*K.q.* subsp. *Quasipneumoniae*, *K. q.* subsp. *Similipneumoniae*), *K. grimontii* and *K. variecola*. (NCBI2019).

## Antimicrobial resistance (AMR) of *Klebsiella* organisms

*Klebsiella* organisms are resistant to multiple antibiotics. This is thought to be a plasmid-

mediated property. They secrete  $\beta$  lactamases enzymes responsible for antibiotic resistance, with genes blaTEM, blaSHV, blaCTX-M, and blaOXA detected globally, facilitating the transfer between different environments, humans, and animals (Khameneh *et al.*, 2019 and Wu *et al.*, 2022). Many factors lead to multidrug resistance and transfer of *Klebsiella* organisms as:

**1-** Length of hospital stay and performance of invasive procedures are risk factors for acquisition as it an opportunistic pathogen that has rapidly spread worldwide causing nosocomial and community-acquired infections (Sarowska *et al.*, 2022; Tian *et al.*, 2023), Due to their colonization to the medical instruments and equipment in hospitals and transmitted through the hands of medical staff and their contact with patients (Pruss *et al.*, 2023). Those Hospital-acquired infections lead to pneumonia, UTI, wound and gastrointestinal infections and primary or secondary bacteremia, The mortality rate of hospital-acquired pneumonia caused by *K. pneumoniae* reach more than 50% (Li *et al.*, 2023). *Klebsiella pneumoniae* causes of nearly 10% of nosocomial infections in Western countries that exhibit multidrug resistance and virulence. Which known for high phenotypic and genetic diversity, in particular regarding antimicrobial-resistance genes (ARGs) a (Chiaverini *et al.*, 2022).

**2-** Food as a vehicle for transmitting antimicrobial-resistant bacteria to humans. MDR *K. pneumoniae* isolates have also been widely detected in milk samples and meat so they transfer from food handlers and consuming unpasteurized milk and raw meat, lead to severe infections such as septicemia and liver abscesses, and occurrence of antimicrobial-resistant strains which cause significant public health risks (ALzubaidi and Alkhafaji 2022), The World Health Organization (WHO) represent AMR of *K. pneumoniae* in food vary according to location, food type, and antibiotic use in veterinary medicine. The WHO has classified carbapenem-resistant and third-generation cephalosporin-resistant Enterobacteriaceae, including *K. pneumoniae*, as critical pathogens needing new treatments, The Centers for Disease Control and Prevention (CDC) have identified *K. pneumoniae* as one of the ESKAPEE pathogens (*Enterococcus faecium*, *Staphylococcus*

*aureus*, *K. pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Enterobacter spp* and *Escherichia coli*), highly concerning drug-resistant organisms with significant public health importance (**World Health Organization (WHO). 2017**).

3– Many virulence genes of *Klebsiella* organisms like Uge (responsible for smooth lipopolysaccharide and capsule synthesis) and Kfu (iron uptake system), These virulence factors, combined with antibiotic resistance, make *klebsiella* a significant threat and frequently produces ESBLs, leading to multidrug resistance (**El Fertas *et al.*, 2013**). Antibiotic resistance was considered a problem to human health, caused by excessive and inappropriate use of antibiotics in human medicine and many sectors (agriculture, animal management and aquaculture) has been increasingly recognized as an important driver of antibiotic resistance. (**Sivaraman *et al.*, 2021**).

The emergence of antimicrobial resistance in, such as the extended-spectrum  $\beta$ -lactamases (ESBL) and AmpC  $\beta$ -lactamases, is threatening the future of the application of  $\beta$ -lactam drugs in both humans and animals. Antimicrobial resistance increases the risk of antimicrobial treatment failure in humans and animals also are transmitted to humans. Therefore, identification of antibiotic susceptibilities and genetic characteristics of ESBL and AmpC  $\beta$ -lactamases-producing *Klebsiella spp.* has an important role in the treatment of pathogenic infections. (**Davis *et al.*, 2015**).

The results of antibiotic sensitivity test showed that the highest resistance was to ampicillin (100%), followed by chloramphenicol (76.7%) and the highest sensitivity was to gentamycin (100%), followed by ciprofloxacin and erythromycin (76.7%), nalidixic (73.33%), and streptomycin (53.4%). (**Ramadan *et al.*, 2023**) which come in agree with (**Chiaverini *et al.*, 2022**) who detect 17 isolates (100%) were resistant at least to one antimicrobial. Regarding  $\beta$ -lactams, all *K. pneumoniae* isolates were resistant to ampicillin, cloxacillin, and cefazolin. All the 16 *K. pneumoniae* isolates were susceptible to aminoglycosides (amikacin, gentamicin, netilmicin, and kanamycin), and **Gomaa (2021)** who found that all *K. pneumoniae* isolates were resistant to ampicillin and amoxicillin-clavulanic acid (100%) followed by

cefepime (72.72%), tetracycline, trimethoprim and trimethoprim/sulphamethoxazole (54.54% each), while they were sensitive to imipenem (82%) followed by aztreonam (55%) then amikacin and azithromycin (45%).

In the study by (**Wu *et al.* 2022**), the MDR rate was 44%, and the prevalence of blaTEM, blaSHV (b-lactam resistance genes), strA, strB, aadA1 (aminoglycoside resistance genes), aac(60)-Ib-cr (resistance gene on quinolones gene) was over 50%. (**Cao *et al.* 2023**) showed strong resistance to  $\beta$ -lactam drugs related to the presence of blaSHV (100%) and blaTEM (65%) genes. It was also found that *K. pneumoniae* isolates carried genes encoding carbapenem resistance (blaNDM-1 - 37%, blaVIM - 18%, blaOXA-10 - 19%). **Yang *et al.* (2021)** found that 71% of *K. pneumoniae* isolates in eastern provinces of China harboured at least one of the antimicrobial resistance genes. Among them, blaSHV(68%), blaCTX-M (17%), aac(60)-Ib (15%), aac(60)-II (3%), aph(30)-I (24%), ant(300)-I (20%) and tetA (30%) were found.

The following antimicrobial resistance genes were identified by (**Massé *et al.*, 2019**): *tetA*, *tetB*, *sulI*, *strA/strB*, and *aadA*. Random amplified polymorphic DNA revealed the majority of our isolates as unrelated and having different patterns, indicating environmental contamination as the primary source of infection. All isolates were shown to be biofilm producers *Klebsiella* isolates showed more than 40% resistance to penicillin, cephalosporin, fluoroquinolone, and aminoglycoside. ESC resistance genes, CTX-M groups (CTX-M-3, CTX-M-15, and CTX-M-65), and AmpC (CMY-2 and DHA-1) were most common in the *K. pneumoniae* strains. Some *K. pneumoniae* carrying CTX-M or AmpC were transferred via IncFII plasmids. Two sequence types, ST709 and ST307, from *K. pneumoniae* were most common (**Lee *et al.*, 2021**).

The prevalence rate of *K. pneumoniae* in milk samples from mastitic cows was 4% (2/50). The antimicrobial susceptibility results showed that *K. pneumoniae* isolates had high resistance rates to ampicillin and ampicillin/clavulanate (100% each) followed by azithromycin, cefepime, and trimethoprim/sulphamethoxazole (91.7% each). Meanwhile, these isolates show high sensitivity levels to chloram-

phenicol (83.3%), Furthermore, 91.7% of *K. pneumoniae* isolates were able to produce the biofilm, where 8.3% was a non-biofilm producer. Out of 11 *K. pneumoniae* isolates, 6 (54.5%), 3 (27.3%) and 2 (18.2%) were moderate, strong and weak biofilm producers, respectively that can be determined by (Ammar et al 2021).

### Prevalence of Klebsiella species from different sources:-

#### From human

Klebsiella species can lead to a wide range of disease states, notably pneumonia, urinary tract infections, sepsis, meningitis, diarrhea, peritonitis and soft tissue infections. The majority of human Klebsiella infections are caused by *K. pneumoniae*, cause serious diseases, including pneumonia, bloodstream infections, sepsis, meningitis, pyogenic liver abscesses, infections of the urinary tract and wounds (Paczosa and Meccas, 2016; Kot et al., 2023). followed by *K. oxytoca*. Which associated with antibiotic-associated hemorrhagic colitis. antibiotic-associated diarrhea, It is postulated that the overgrowth of cytotoxin-producing strains of *K. oxytoca* in the colon during antibiotic therapy can cause direct mucosal damage and hemorrhagic changes The right colon is preferentially affected, but disease may extend to the transverse and descending segments. Mucosal edema, erosion, and longitudinal ulcers are also typical Infections are more common in the very young, very old, and those with other underlying diseases, such as cancer and most infections involve contamination of an invasive medical device (Nicole and Panarelli 2024)

#### Klebsiella From animal

Klebsiella spp cause economic problems in farm animals as causing mastitis in dairy cows and affect animal welfare due to pain from infection, Also cause respiratory disorders in ruminants and neonatal septicemia in calves (Cheng et al., 2020). Klebsiella species could be isolated from different sources most of them were from pig, cattle, pork and milk and the rest of isolates were isolated from vegetables, pets, livestock and farm animals (Klaper et al., 2021). Infections with Klebsiella spp. cause a variety of syndromes in livestock, the most important being endometritis, infertility and abor-

tion in mares, mastitis in cows and sows, and neonatal septicaemia, particularly in foals.. *K. pneumoniae* could be isolated by (Ramadan et al., 2023) from clinically diseased cattle and buffaloes in percent of 10.5% and 8.33% from cattle and buffaloes respectively (nasal swabs, milk samples, anal swabs) Klebsiella species can be isolated from clinical mastitis cases in Canada, were identified to *Klebsiella pneumoniae* (n = 40), *Klebsiella oxytoca* (n = 9), *Raoultella ornithinolytica* (n = 2), and *Raoultella planticola* (n = 2). *Raoultella*, a genus closely related to Klebsiella (Massé et al., 2020). It is isolated in 2 to 9% of milk samples from clinical mastitis cases by (Levison et al., 2016), it Can cause mammary gland infection characterized by severe clinical signs a major decrease in milk production and leads to economic losses. Affected animals are frequently removed from the herd (Sugiyama et al., 2022; Fuenzalida and Rugg, 2019). The prevalence of Klebsiella from clinically mastitic cows was 36% of milk samples positive detected by (Fu et al., 2022), also Klebsiella spp. in clinical bovine mastitis showed 7% higher than in subclinical cases (4%) detected by (Liu et al. 2022), The prevalence of *K. pneumoniae* in the northern areas of China was 3% in 2018 and 2019 (Song et al., 2022), 10% (Yang et al., 2021) or 15% (Cao et al., 2023) in the eastern provinces (Jiangsu and Shandong) the prevalence was 27% (Wu et al., 2022). The prevalence of *K. pneumoniae* in China indicates that these bacteria pose an increasing hazard to the dairy industry.

Bovine mastitis caused by Klebsiella spp is difficult to be controlled, decrease milk production, increase mortality rate and this micro-organism has a zoonotic importance, overall, *K. pneumoniae* strains were detected in 90 (81.8%) samples, 23 (25.6%) were from chicken, 32 (35.6%) from bovine samples and 35 (38.9%) from pork. Moreover, 23 of 35 (65.7%) chicken samples, 32 of 35 (91.4%) bovine samples, and 35 of 40 (87.5%) pork samples were positive for *K. pneumoniae* (Langoni et al., 2015).

*K. pneumoniae* become a source of human infection due to its presence in livestock, retail meats, and vegetables, Contaminated food including vegetables, raw meat, and dairy products (Riwu et al., 2022). on dairy farms organ-

samples from West Bengal and Himachal Pradesh, respectively, were positive for ESBL-producing *K. pneumonia* (Bandyopadhyay *et al.*, 2018). A multi-state study in India found that 4.4%, 13%, and 6% of bovine milk samples from West Bengal, Jharkhand, and Mizoram, respectively, contained ESBL-producing *K. pneumoniae* (Koovapra *et al.*, 2016). In Lebanon, 23.4% of milk samples from healthy cattle tested positive for *K. pneumoniae* using MALDI-TOF-MS, and all were ESBL producers.

*K. pneumoniae* has been found in milk and milk products including camel's milk, raw cow's milk, raw fermented milk, Ricotta cheese, soft cheese, full cream milk powder, milk powder infant formula, cereal baby food, and growing-up formula. Out of 234 samples, 16 (6.8%) exhibited mucoid colonies indicative of *K. pneumoniae*. This identification was confirmed using 16S rRNA molecular techniques. Antibiotic susceptibility tests on 12 of the isolates showed resistance to more than eight antibiotics, with two isolates producing metallo-beta-lactamase (MBL). (Azwai *et al.*, 2024).

***K. pneumoniae* from Fruits and Vegetables:-** A South Korean study found that 8.5% of ready-to-eat (RTE) vegetables contained *K. pneumoniae*, with 69% of the isolates carrying blaTEM-1, 94% carrying blaSHV, 50% carrying blaCTX-M-14, and 19% carrying blaCTX-M-15 (He *et al.*, 2016). In Oman, 13 *K. pneumoniae* isolates were recovered from 105 fresh raw vegetable and fruit samples (Al-Kharousi *et al.*, 2016). In Algeria, 13 third-generation cephalosporin-resistant *K. pneumoniae* isolates from fresh fruits and vegetables were found to harbor sulfonamide, quinolone,  $\beta$ -lactam, and aminoglycoside resistance genes (Mesbah Zekar *et al.*, 2020). *K. pneumoniae* has also been detected in sugarcane juice, showing resistance to antimicrobials like gentamicin, kanamycin, and neomycin. In China, a mcr-1 carrying *K. pneumoniae* was isolated from fresh fruit samples, also containing resistant genes blaSHV-110, tetA, and qnrS1 (Yang *et al.*, 2019). A Singapore study found *K. pneumoniae* in 15% of RTE foods and 45% of raw food samples like vegetables and meat, although only 7% of RTE foods carried a virulence gene (Hartantyo *et al.*, 2020). In

Ethiopia, 12.3% of food handlers had a fecal carriage of *K. pneumoniae* (Eibach *et al.*, 2018). European studies reported *K. pneumoniae* in ready-to-eat raw vegetables like carrots, tomatoes, and pumpkins, with resistance genes identified through whole genome sequencing (Centorotola *et al.*, 2021). Additionally, *K. pneumoniae* was isolated from cheese manufacturing plants and raw materials like milk powder and cheese cans (Giri *et al.*, 2021). A 2022 multicentric study in Europe found high levels of *K. pneumoniae* in chicken meat (60%) and salads (30%) (Rodrigues *et al.*, 2022).

## 1) Microbiology of klebsiella:-

### a) Morphology and Culture characters:-

Klebsiella were gram negative bacilli arranged single or in short chain, can grow in many media as Tryptic soya agar appeared as large, smooth, raised, and cream yellow colonies. While on MacConkey agar appears as large, pink, round, smooth, and mucoid colony. On XLD yellow mucoid colony, on Brilliant green agar yellow-green colonies, on EMB violet metallic mucoid colonies and on blood agar non hemolytic colonies were observed. (Markey *et al.* 2013, He *et al.* 2022; Ramadan *et al.*, 2023).

### b) Virulence factors:-

*K. pneumoniae* pathogenicity is associated with several virulence factors including capsules, siderophores, LPSs, and pili that help it to invade the host's immune system these virulence factors include capsules, exo-polysaccharides, lipo-polysaccharides (LPSs), adhesins, and iron uptake systems. These factors cause multiple antibiotic resistance and nosocomial infections in humans. The capsule is a significant virulence factor, involved in two pathogenic mechanisms, that is, the protection of bacteria from phagocytosis and direct inhibition of the vulnerable host response. Several capsule types (K), especially, K1, K2, K54, K57, K20, and K5, are associated with pyogenic liver abscess, septicemia, and pneumonia. (Wei *et al.*, 2016, Cheng *et al.*, 2020, Parrott *et al.*, 2021).

Capsular antigen can prevent *K. pneumoniae* from being recognized by the host immune system through some immune escape mechanisms such as antiphagocytosis, inhibition of

ic bedding materials and cattle feces are sources of *Klebsiella* species, which lead to contamination of dairy products (Cheng *et al.*, 2021).

### ***K. pneumoniae* from Meat**

*K. pneumoniae* has been detected in various meat sources worldwide, particularly in beef, pork, chicken, mutton, and chevon. Studies have shown a prevalence of *K. pneumoniae* in chicken ranging from 3.6% to 60%. In one study, 31 out of 70 samples of beef, turkey, and chicken from grocery stores tested positive for *K. pneumoniae* and all isolates were resistant to antibiotics like ampicillin, tetracycline, streptomycin, gentamicin, and kanamycin. The most commonly detected resistance genes were *aadA1*, *tetA*, *blaSHV-1*, and *blaTEM-1* (Kim *et al.*, 2005). In Turkey, 21 *K. pneumoniae* isolates were recovered from 60 raw meat and chicken samples, with 28.3% being ESBL-producers, exhibiting resistance to extended-spectrum  $\beta$ -lactam antibiotics. Additionally, 55%, 53%, and 47% of isolates exhibited siderophore production, serum resistance, and haemolytic activity, respectively (Gundogan *et al.*, 2007).

In the USA, a study on *K. pneumoniae* from food and clinical samples found that 32% of meat isolates were resistant to multiple drugs like ampicillin, gentamicin, and tetracycline, a higher percentage than in clinical samples (Diab 2017). In Ghana, a study found 81 ESBL-producing isolates out of 200 poultry meat samples, with 35 being *K. pneumoniae*, and *blaCTX-M-15* detected in 86% of the isolates. The common sequence types were ST2570, ST147, and ST15 (Gaffer 2019). In Europe, a multi-centric study reported that 60% of chicken samples harbored *K. pneumoniae* (Rodrigues, 2022), while in Turkey, 3.6% of raw chicken meat samples tested positive for ESBL-producing *K. pneumoniae* (Tekiner and Özpınar, 2016).

Studies from Greece, South Africa, Iraq, and Assam reported high prevalence rates of *K. pneumoniae* in meat samples, with Greece showing 82% in pork, chicken, and beef (Theocharidi *et al.*, 2022), South Africa 32% in retail beef (Montso *et al.*, 2019), Iraq 76%

in retail beef (Klaif *et al.*, 2019), and Assam 21.43% in beef (Chauhan *et al.*, 2013). In Anand, Gujarat, 57% of chevon samples tested positive for *K. pneumoniae* (Prajapati *et al.*, 2022), while in Pakistan, the prevalence was 36.4% in beef samples (Junaid *et al.*, 2022). Another study from Iraq found a 56% prevalence in retail beef samples (Al-Dabbagh 2022). In Indonesia, 7.8% of chicken cloacal swabs were positive for *K. pneumoniae*, compared to 28% in a similar study from China (Hartantyo *et al.*, 2020). In Gujarat, India, 6% of chicken meat samples tested positive for *K. pneumoniae* (Modh *et al.*, 2021).

### ***K. pneumoniae* from Street foods**

A study in China tested various retail food samples, including meatballs and raw meat from different livestock species, for the presence of *K. pneumoniae*. They found a high percentage of virulence genes such as *fimH*, *ureA*, *wabG*, and *uge*. The isolates exhibited high resistance to ampicillin, streptomycin, piperacillin, and tetracycline, with nearly 18% being multidrug resistant (Zhang *et al.*, 2018). Similarly, a study in India revealed that 28.12% of paani puris and chaats were positive for *K. pneumoniae*, which was more common (27.12%) than *Escherichia coli* (22.88%) in retail foods. The isolates showed high resistance to ampicillin, cefepime, cefuroxime, and cefotaxime. Additionally, eight isolates were metallo-beta-lactamase producers, and two isolates were positive for all three ESBL genes: *blaCTX-M*, *blaSHV*, and *blaTEM* (Giri *et al.*, 2021).

In Shijiazhuang city, China, 9.9% of 998 food samples tested were positive for *K. pneumoniae*. In Benin, nearly 20% of 216 street food samples were positive for *K. pneumoniae*, with 27% of isolates resistant to imipenem and 20% carrying ESBL genes (Moussé *et al.*, 2016).

### ***K. pneumoniae* from Milk and Milk product**

ESBL-producing *K. pneumoniae* has been found in raw milk and various milk products such as khoa, ice cream, kareish, and domiati cheese in studies from India (Bobbadi *et al.*, 2020), Indonesia (Budiarso *et al.*, 2021), and Egypt (Gelbíčová *et al.*, 2021). In India, a study reported that 3% and 27% of bovine milk

early inflammatory response, neutralization of antimicrobial peptides to reduce the body's immune response (Paczosa and Mecsas, 2016), also these bacteria can absorb the iron of the host via four siderophores such as aerobactin, salmochelin, enterobactin and yersiniabactin for metabolism and enhance the virulence to cause infection (Wang *et al.*, 2020).

*K. pneumoniae* has fimbriae : type 1 (fim) and type 3 (mrk) fimbriae. Type 1 fimbriae can enhance virulence by adhering to mucosal or epithelial surfaces and type 3 fimbriae adhere to the cell surface and promote biofilm formation (Schroll *et al.*, 2010). Lipid A, a component of lipopolysaccharide, reduces the inflammatory response during *K. pneumoniae* infection and prevents the bactericidal effect of cationic antimicrobial peptides. O antigen is the outermost subunit of LPS, which eliminates the lysis of bacteria by the complement membrane attack complex (Paczosa and Mecsas, 2016). In a study by (Schonborn *et al.* 2017), 84% of *Klebsiella* spp. isolates were shown to produce visible biofilm formation in a tube method, biofilm formation for this pathogen in isolates recovered from bovine mastitis cases (Massé *et al.*, 2019), This results is coordinated with that reported by (Massé *et al.* 2020). While, (Gomaa 2021) stated that 81.81% of *K. pneumoniae* isolates could produce biofilms, those categorized as strong (33.33%), moderate (22.22%) or weak (44.44%) biofilm producers, whereas 18.18% of the isolates were non-biofilm producers.

The *ecpA* gene was detected in *K. pneumoniae* strains from 14 (46.7%) chicken and 16 (53.3%) bovine specimens. Moreover, the *fimH-1* and *mrkA* genes, encoding type 1 and type 3 fimbrial adhesins, were present in 15 (16.7%) and 65 (72.2%) strains of *K. pneumoniae* isolates, respectively. Among the 15 samples, the *fimH-1* gene was present in 33.3% of the three categories of meat Products. Among the 65 isolates, the *mrkA* gene was present in 50 of the chicken and bovine meat products and 15 of the pork meat products (Theocharidi *et al.*, 2022).

*K. pneumoniae* can form biofilm which is one of the crucial conditions for maintaining its activity. and it accumulates in such cells em-

bedded in the self-generated matrix of the extracellular polymeric substance Extracellular polymeric substances are complex structures containing polysaccharides, proteins, and DNA. Many genes responsible for formation biofilm as *blaNDM*, *fabZ*; *lpxC* Biofilm homeostasis,, *YfgL (BamB)* biofilm formation; transcriptional expression of type 1 pili and *KpOmpA* Cell-cell recognition, adhesion, and immune response; pathogenicity (Guoying Wang *et al.* 2020).

Most clinically apparent *K. pneumoniae* biofilm is formed on the catheter and the inner surface of internal devices *K. pneumoniae* biofilm can lead to colonization in the respiratory, gastrointestinal, and urinary tracts, as well as the development of invasive infections (especially in immune-deficient patients). The development of *K. pneumoniae* biofilm on the surface of hard objects undergoes the adhesion of cells, the formation of small colonies, maturation, and the propagation as ultimately free-living cells.

The most important surface structures of *K. pneumoniae* involved in the formation process are type 3 pili and capsular polysaccharides (CPs) Pili mediate steady adhesion, while CPs ultimately affect biofilm structure and intercellular communication. Given the dynamics of biofilm formation and the variability of environmental stimuli, embedded bacterium must have the ability to rapidly and extensively change gene expression. Transcriptional regulation is regulated by quorum sensing, a system coordinating the signals and responses that control gene expression in a microbial population. The putative quorum-sensing-related regulators and autoinducers in *K. pneumoniae* have been identified, but the relevant available data is still incomplete (Clegg *et al.*, 2016). *K. pneumoniae* with biofilm is protected from the host immune response, in part. This matrix inhibits the proximity of antibodies and antimicrobial peptides, and reduces the effects of complement and phagocytosis. Mutations in some specific genes of *K. pneumoniae* can also affect the function of biofilm. Found that *fabZ* and *lpxC* mutations lead to *lpxC* inhibitor-dependent growth of *K. pneumoniae*, which leads to the loss of biofilm homeostasis (Mostafavi *et al.*, 2018). In recent

years, the research on the outer membrane protein of *K. pneumoniae* has attracted the attention of researchers. **Hsieh *et al.* (2016) reported** that YfgL (BamB) lipoprotein is involved in the biofilm formation of *K. pneumoniae* and the transcriptional expression of type 1 pili, which is critical for the anti-phagocytosis of *K. pneumoniae* in vivo (**Hsieh *et al.*, 2016**). Besides this, *K. pneumoniae*'s outer membrane protein A (KpOmpA) is reported to be involved in cell adhesion and cell-cell recognition, as well as immune response of host. Meanwhile, the L3 site on the KpOmpA surface may be related to pathogenicity of *K. pneumoniae* (**Saurel *et al.* 2017**). Oxidative stress may oxidize and destroy the biofilm of *K. pneumoniae*, resulting in the loss of major membrane proteins and activity of *K. pneumoniae*

### Plant extracts

Plant-derived chemicals are a large group of chemical compounds that have been found naturally in plants. The wide uses of these compounds are in the form of antioxidant, antibacterial, and antifungal activities. They enable the application of older antibiotics by increasing their efficacy and avoid the development of resistance. they will be classified into many major groups that include alkaloids, sulfur-containing compounds, terpenoids, and polyphenols (**Khameneh *et al.*, 2019**).

This approach provide a safe and low-cost medicinal plant having antibacterial activities with a promising future. More than half a million plants worldwide have medical uses essential to treat or prevent many infections with less toxicity and side effects and could be a good substitute for traditional synthetic chemical antibiotics and overcome multidrug-resistant bacteria, The most important of these bioactive constituents are alkaloids, tannins, flavonoids, and phenol, all of which are accoutered for new antibacterial agents, It is believed that crude extracts from some medicinal plants are more biologically active than isolated compounds due to their synergistic effects. (**Voon *et al.* 2012**).

Plant extracts have shown promising antibacterial effects. This review focuses on the activities of some plant extract like green tea, cinna-

mon and *Rhazya stricta* leaf extracts against *K. pneumoniae*.

### The *Rhazya stricta*

The *Rhazya stricta* leaf extracts exerted antibacterial and antibiofilm effects against *K. pneumoniae*. Both ethanolic and methanolic extracts, rich in flavonoids and phenolic acids like quercetin and caffeic acid, were effective in inhibiting bacterial growth and biofilm formation. The ethanolic extract showed slightly better antibacterial and antibiofilm activities, with up to 98.7% biofilm inhibition, due to higher concentrations of compounds like quinol and p-coumaric acid. These findings suggest that *R. stricta* extracts could serve as promising way to cotrol *K. pneumoniae* infections (**Hassan *et al.*, 2023**).

### Green tea extract

Green tea extract (GTE) has a natural antimicrobial agent against *K. pneumoniae* (**Aneja and Gianfagna, 2001**). it contains compounds like catechins such as epicatechin gallate (ECg) and epigallocatechin gallate (EGCg), which disrupt bacterial cell membranes and inhibit essential bacterial enzymes (**Zhao *et al.*, 2001**). Studies found that higher doses of GTE, such as 5 mL lead to significantly decrease in bacterial numbers. GTE can be used as natural solution to controlling contamination of *K. pneumoniae* in raw chicken meat (**Kaderi *et al.*, 2023**).

### Cinnamon extract

Cinnamon extract, rich in compounds like cinnamaldehyde and eugenol, these compounds target and disrupt the bacterial cell wall and membrane, leading to structural damage and cell death. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) for cinnamon extract were 500 µl/ml, demonstrating its effectiveness as a bactericidal agent. (**Ouattara *et al.*, 1997**).

Cinnamon extract was more effective over a short duration within 6–8 hours. Similarly, green tea extract caused rapid cell death due to the hydrophobic nature of its compounds, which disrupt bacterial membranes, rendering them more permeable (**El-Farmawi *et al.* 2014, Sikkema *et al.* 1995**).

### Lemon extract

Lemon extract, particularly from its peel, has shown antimicrobial activity against *K. pneumoniae* (Nada *et al.*, 2024). The bioactive compounds in lemon, such as flavonoids, essential oils, and limonoids, disrupt bacterial cell walls and inhibit growth (Harfouch *et al.* 2019). Studies have demonstrated that ethanolic and methanolic extracts of lemon peel are more effective than aqueous extracts. However, *K. pneumoniae* tends to exhibit higher resistance compared to Gram-positive bacteria (Hindi & Chabuck 2013).

### Conclusion

*Klebsiella* spp is a opportunistic bacterium that can survive and difficult to eradicate once present in the food system. To prevent its spread, it is essential to implement good hygiene practices and maintain proper cooking and storage temperatures. The global problem of drug-resistant *K. pneumoniae* is a major concern due to its ability to infect various human tissues, including critical organs. *K. pneumoniae*'s virulence mechanisms remain unclear, therefore application of plant extracts to avoid bacterial resistance and overcoming this virulence is very important for human and animal health also the antimicrobial resistance and *K. pneumoniae* infections requires cooperation between medical, veterinary, pharmacological, microbiological, and environmental sectors for inhibiting the growth of pathogenic microorganisms and enhancing food safety.

### References

- Adefegha, S.A. (2019). Antibiotics and Drug Pharmacology. Acta Scientific Pharmaceutical Sciences, [online] 3(11), pp.43–49.
- Al-Dabbagh, S.Y. (2022). Molecular characterization of extended spectrum beta-lactamase producing *Klebsiella pneumoniae* isolated from cows in Mosul city, Iraq. Iraqi Journal of Veterinary Sciences, Vol. 36, No. 2, (375-380).
- Al-Kharousi, Z.S.; Guizani, N.; Al-Sadi, A.M.; Al-Bulushi, I.M. and Shaharouna, B. (2016). Hiding in fresh fruits and vegetables: opportunistic pathogens may cross geographical barriers. International Journal of Microbiology, Feb; 2016.
- ALzubaidi, S.J. and Alkhafaji, M.H. (2022). Molecular detection of bla SHV gene in clinical and foodborne *Klebsiella pneumoniae* isolates. Euphrates Journal of Agriculture Science. 2022;14(4).
- Ammar, A.M.; Marwa, I. Abd El-Hamid1 and Noha, A. Gomaa (2021). Prevalence, Antimicrobial Resistance and Biofilm Formation of *Klebsiella Pneumoniae* Isolated from Human and Cows Zagazig Veterinary Journal, Faculty of Veterinary Medicine, Zagazig University, 44511, Egypt. Volume 49, Number 2, p. 27-41.
- Aneja, M. and Gianfagna, T. (2001). Induction and accumulation of caffeine in cocoa leaves. Physiological and Molecular Plant Pathology, 59: 13–16..
- Azwai, S.M.; Aml, F. Lawila; Hanan, L. Eshamah; Jihan, A. Sherif; Samira, A. Farag; Hesham, T. Naas; Aboubaker, M. Garbaj; Allaaeddin, A. El Salabi; Fatim, T. Gammoudi and Ibrahim, M. Eldaghayes (2024). Antimicrobial susceptibility profile of *Klebsiella pneumoniae* isolated from some dairy products in Libya as a foodborne pathogen, Vet World 2024 May 22;17(5):1168–1176.
- Bandyopadhyay, S.; Banerjee, J.; Bhattacharyya, D.; Samanta, I.; Mahanti, A. and Dutta, T.K. (2018). Genomic identity of fluoroquinolone-resistant bla CTX-M-15-Type ESBL and pMampC  $\beta$ -lactamase producing *Klebsiella pneumoniae* from buffalo milk, India. Microbial Drug Resistance, 24(9):1345-53.
- Bobbadi, S.; Kiranmayi, C.B.; Nelapati, S.; Tumati, S.R.; Kandhan, S. and Gottapu, C. (2020). Occurrence and genetic diversity of ESBL producing *Klebsiella* species isolated from livestock and livestock products. Journal of Food Safety, 40(1):e12738.
- Budiarso, T.Y.; Amarantini, C. and Pakpahan, S. (2021). Biochemical identification and molecular characterization of *Klebsiella pneumoniae* isolated from street foods and drinks in Yogyakarta, Indonesia using 16S rRNA gene. Biodiversitas, 22(12).
- Cao, W.; Xu, Y.; Huang, Y. and Xu, T. (2023). Isolation of pathogenic bacteria from dairy cow mastitis and correlation of biofilm formation and drug resistance of *Klebsiella pneumoniae* in Jiangsu, China. Agriculture

- 13, 1984.
- Centorotola, G.; Cornacchia, A.; Marfoggia, C.; Saletti, M.A.; Ciarrocchi, A. and Del Matto, I. (2021).** *Klebsiella pneumoniae* in vegetable products: antimicrobial resistance and consumer health risk. *European Journal of Public Health*, 31(Supplement\_3): cka-b165-630.
- Chauhan, S.; Farooq, U.; Singh, V. and Kumar, A.J. (2013).** Determination of prevalence and antibacterial activity of ESBL (Extended Spectrum Beta-lactamases) producing *Klebsiella* species isolated from raw milk of Doon Valley in India. *International Pharma Bio Sciences*, 4(1): 417-423.
- Cheng, F.; Li, Z.; Lan, S.; Liu, W.; Li, X.; Zhou, Z.; Song, Z.; Wu, J.; Zhang, M. and Shan, W. (2018).** Characterization of *Klebsiella pneumoniae* associated with cattle infections in southwest China using multi-locus sequence typing (MLST), antibiotic resistance and virulence-associated gene profile analysis. *Braz J Microbiol* 49 (1), 93-100.
- Cheng, J.; Zhou, M.; Nobrega, D.B.; Cao, Z.; Yang, J.; Zhu, C.; Han, B. and Gao, J. (2021).** Virulence profiles of *Klebsiella pneumoniae* isolated from 2 large dairy farms in China. *J. Dairy Sci.*, 104(8): 9027–9036.
- Cheng, J.; Zhang, J.; Han, B.; Barkema, H.W.; Cobo, E.R.; Kastelic, J.P.; Zhou, M.; Shi, Y.; Wang, J. and Yang, R. (2020).** *Klebsiella pneumoniae* isolated from bovine mastitis is cytopathogenic for bovine mammary epithelial cells. *J. Dairy Sci.* 103, 3493–3504.
- Chiaverini, A.; Cornacchia, A.; Centorotola, G.; Tieri, E.E.; Sulli, N.; Del Matto, I.; Iannitto, G.; Petrone, D.; Petrini, A. and Pomilio, F. (2022).** Phenotypic and Genetic Characterization of *Klebsiella pneumoniae* Isolates from Wild Animals in Central Italy. *Animals*, 12(11), 1347.
- Clegg, S. and Murphy, C.N. (2016).** Epidemiology and Virulence of *Klebsiella pneumoniae*. *Microbiol. Spectr.* 2016;4 doi: 10.1128/microbiolspec.UTI-0005-2012.
- Davis, G.S. and Price, L.B. (2016).** Recent research examining links among *Klebsiella pneumoniae* from food, food animals, and human extraintestinal infections. *Current Environmental Health Reports* 3, 128–135.
- Diab, M.; Hamze, M.; Bonnet, R.; Saras, E.; Madec, J.Y. and Haenni, M. (2017).** OXA-48 and CTX-M-15 extended-spectrum beta-lactamases in raw milk in Lebanon: epidemic spread of dominant *Klebsiella pneumoniae* clones. *Journal of Medical Microbiology*, 66 (11): 1688-1691.
- Eibach, D.; Dekker, D.; Boahen, K.G.; Akenten, C.W.; Sarpong, N. and Campos, C.B. (2018).** Extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in local and imported poultry meat in Ghana. *Veterinary Microbiology*, 217: 7-12.
- El Fertas-Aissani, R.; Messai, Y.; Alouache, S. and Bakour, R. (2013).** Virulence profiles and antibiotic susceptibility patterns of *Klebsiella pneumoniae* strains isolated from different clinical specimens. *Pathol. Biol. (Paris)*;61(5):209–216. doi: 10.1016/j.patbio.2012.10.004.
- EL-Farmawi, D.; Olama, Z. and Holail, H. (2014).** The antibacterial effect of some natural bioactive materials against *Klebsiella pneumoniae* and MRSA. *International Journal of Current Microbiology and Applied Sciences*, 3(3): 576–588. Available at IJCMAS.
- Fuenzalida, M.J. and P.L. Ruegg (2019).** Negatively controlled, randomized clinical trial to evaluate intramammary treatment of nonsevere, gram-negative clinical mastitis. *J. Dairy Sci.* 102:5438–5457.
- Fu, S.; Wen, C.; Wang, Z.; Qiu, Y.; Zhang, Y.; Zuo, J.; Xu, Y.; Han, X.; Luo, Z.; Chen, W. and Miao, J. (2022).** Molecular epidemiology and antimicrobial resistance of outbreaks of *Klebsiella pneumoniae* clinical mastitis in Chinese dairy farms. *Microbiology Spectrum* 21, e0299722.
- Gaffer, W.; Gwida, M.; Samra, R. A. and Al-Ashmawy, M. (2019).** Occurrence and molecular characterization of extended-spectrum beta-lactamase-producing Enterobacteriaceae in milk and some dairy products. *Slov. Vet. Zb.*, 56.
- Gelbíčová, T.; Kořená, K.; Pospíšilová-Hlucháňová, L.; Straková, N. and Karpíšková, R. (2021).** Dissemination and characteristics of *Klebsiella* spp. at the pro-

- cessed cheese plant. Czech Journal of Food Sciences, 39(2): 113-121.
- Giri, S.; Kudva, V.; Shetty, K. and Shetty, V. (2021).** Prevalence and characterization of extended-spectrum  $\beta$ -lactamase-producing antibiotic-resistant *Escherichia coli* and *Klebsiella pneumoniae* in ready-to-eat street foods. Antibiotics, 10(7): 850.
- Gomaa, N.A. (2021).** Prevalence, antimicrobial resistance, and biofilm formation of *Klebsiella pneumoniae* isolated from human and cows. Zagazig Veterinary Journal . 41-27 : (49)
- Gundogan, N. and U. Yakar (2007).** Siderophore production, serum resistance, hemolytic activity and extended spectrum beta lactamase– producing *Klebsiella* species isolated from milk and milk products. J. Food Saf. 3:251–260.
- Guoying Wang, Guo Zhao, Xiaoyu Chao, Longxiang Xie and Hongju Wang (2020).** The Characteristic of Virulence, Biofilm and Antibiotic Resistance of *Klebsiella pneumonia* Int. J. Environ Res Public Health 28;17(17):6278.
- Harfouch, R.M.; Janoudi, H.; Muhammad, W.; Hammami, A. and Chouman, F. (2019).** In Vitro Antibacterial Activity of Citrus limon Peel Extracts Against Several Bacterial Strains. Journal of Chemical and Pharmaceutical Research, 11(7): 48–51.
- Hartantyo, S.H.P.; Chau, M.L.; Koh, T.H.; Yap, M.; Yi, T. and Cao, D.Y.H. (2020).** Foodborne *Klebsiella pneumoniae*: virulence potential, antibiotic resistance, and risks to food safety. Journal of Food Protection, 83 (7): 1096-1103.
- Hassan, M.M.; Albogami, B.; Mwabvu, T.; Awad, M.F.; Kadi, R.H.; Mohamed, A.A.; Al-Orabi, J.A.; Hassan, M.M. and El-sharkawy, M.M. (2023).** The Antibacterial Activity of *Rhazya stricta* Extracts against *Klebsiella pneumoniae* Isolated from Some Soil Invertebrates at High Altitudes. Molecules, 28(8): 3613. Available at MDPI.
- He, T.; Wang, Y.; Sun, L.; Pang, M.; Zhang, L. and Wang, R. (2016).** Occurrence and characterization of bla NDM-5-positive *Klebsiella pneumoniae* isolates from dairy cows in Jiangsu, China. J. Antimicrob. Chemother. 2016; 72(1): 90-94.
- Hindi, N.K.K. and Chabuck, Z.A.G. (2013).** Antimicrobial Activity of Different Aqueous Lemon Extracts. Journal of Applied Pharmaceutical Science, 3(6): 74–78.
- Hsieh, P.F.; Hsu, C.R.; Chen, C.T.; Lin, T.L. and Wang, J.T. (2016).** The *Klebsiella pneumoniae* YfgL (BamB) lipoprotein contributes to outer membrane protein biogenesis, type-1 fimbriae expression, anti-phagocytosis, and in vivo virulence. Virulence. 2016;7:587–601. doi: 10. 1080/ 21505594. 2016.1171435.
- Junaid, K.A.; Hasan, Ejaz a; Sonia, Younas b; Awadh, Alanazi a; Humaira, Yasmeen c and Abdul, Rehman d (2022).** Detection of *Klebsiella pneumoniae* antibiotic-resistant genes: An impending source of multidrug resistance dissemination through raw food Saudi Journal of Biological Sciences (29) 3347–3353.
- Kaderi, K.F.; Islam, M.S.; Sarker, T.; Islam, S.S.; Mondol, D.; Faruk, M.O. and Biswas, G. (2023).** Study on the efficacy of green tea extract on *Staphylococcus aureus* and *Klebsiella pneumoniae* of raw chicken meat. Meat Research, 3(1): Article 45. ISSN: 2790-1971.
- Kakatkar, A.; Gautam, R.; Godambe, P.L. and Shashidhar, R. (2017).** Culture dependent and independent studies on emerging food-borne pathogens Cronobacter sakazakii, *Klebsiella pneumoniae* and *Enterococcus faecalis* in Indian food. International Food Research Journal 24, 2645–2651.
- Khameneh, B.; Iranshahy, M.; Soheili, V. and Fazly Bazzaz, B.S. (2019).** Review on plant antimicrobials: a mechanistic viewpoint. Antimicrobial Resistance & Infection Control, 8(1).
- Kim, S.H.; Wei, C.I.; Tzou, Y.M. and An, H. (2005).** Multidrug-resistant *Klebsiella pneumoniae* isolated from farm environments and retail products in Oklahoma. Journal of Food Protection, 68(10): 2022-2029.
- Kim, H.S.; Chon, J.W.; Kim, Y.J.; Kim, D.H.; Kim, M.S. and Seo, K.H. (2015).** Prevalence and characterization of extended-spectrum- $\beta$ -lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in ready-to-eat vegetables. International Journal of Food Microbiology, 207: 83-86.

- Klaif, S.F.; Naser, H.H. and Sadeq, J.N. (2019). The genetic relationship for *Klebsiella pneumoniae* isolated from human urinary tract and beef. Iraqi Journal of Veterinary Sciences, 33(1): 75-80.
- Klaper, K.; Hammerl, J.A.; Rau, J.; Pfeifer, Y. and Werner, G. (2021). Genome-Based Analysis of *Klebsiella* spp. Isolates from Animals and Food Products in Germany. Pathogens (Basel, Switzerland) 10, 2013-2017.
- Koovapra, S.; Bandyopadhyay, S.; Das, G.; Bhattacharyya, D.; Banerjee, J. and Mahanti, A. (2016). Molecular signature of extended spectrum  $\beta$ -lactamase producing *Klebsiella pneumoniae* isolated from bovine milk in eastern and north-eastern India. Infection, Genetics and Evolution, 44: 395-402.
- Kot, B.; Piechota, M.; Szweda, P.; Mitrus, J.; Wicha, J.; Grużewska, A. and Witeska, M. (2023). Virulence analysis and antibiotic resistance of *Klebsiella pneumonia* isolates from hospitalised patients in Poland. Scientific Reports 17, 4448.
- Kowalczyk, J.; Czokajło, I.; Gan'ko, M.; S' mialek, M. and Koncicki, A. (2022). Identification and antimicrobial resistance in *Klebsiella* spp. isolates from turkeys in Poland between 2019 and 2022. Animals (Basel) 15, 3157.
- Langoni, H.; Guiduce, M.V.S.; Nobrega, D.B.; Silva, R.C.; Richini-Pereira, V.B. and Salina, A. (2015). Research of *Klebsiella pneumoniae* in dairy herds. Pesqui Vet Brasil 2015; 35(1):9–12; <https://doi.org/10.1590/S0100-736X2015000100003>
- Lee, C.R.; Lee, J.H. and Park, K.S. (2017). Antimicrobial resistance of hypervirulent *Klebsiella pneumoniae*: epidemiology, hypervirulence-associated determinants, and resistance mechanisms. Front Cell Infect Microbiol.;7:483. doi:10.3389/fcimb. 2017.00483.
- Levison, L.J.; E.K. Miller-Cushon; A.L. Tucker; R. Bergeron; K.E. Leslie; H.W. Barkema and T.J. DeVries (2016). Incidence rate of pathogen-specific clinical mastitis on conventional and organic Canadian dairy farms. J. Dairy Sci. 99:1341–1350.
- Li, Y.; Kumar, S.; Zhang, L.; Wu, H. and Wu, H., 2023. Characteristics of antibiotic resistance mechanisms and genes of *Klebsiella pneumoniae*. Open Medicine 18,20230707.
- Liu, K.; Zhang, L.; Gu, X. and Qu, W. (2022). The prevalence of *Klebsiella* spp. Associated with bovine mastitis in China and its antimicrobial resistance rate: a meta analysis. Frontiers in Veterinary Science 24, 757504.
- Massé, J.; Dufour, S. and Archambault, M. (2020). Characterization of *Klebsiella* isolates obtained from clinical mastitis cases in dairy cattle. J Dairy Sci 103, 3392-3400.
- Mesbah Zekar, F.; Granier, S.A.; Touati, A. and Millemann, Y. (2020). Occurrence of third-generation cephalosporins-resistant *Klebsiella pneumoniae* in fresh fruits and vegetables purchased at markets in Algeria. Microbial Drug Resistance, 26(4): 353-359.
- Modh, K.S.; Parmar, B.C.; Chaudhary, J.H.; Bhandari, B.B.; Nayak, J.B.; Thakur, S.; Pargi, Z. B. and Patel, N.M. (2021). Molecular detection of *Klebsiella* spp. from poultry meat. Indian Journal of Pure and Applied Biosciences, 9(1): 511-518.
- Montso, K.P.; Dlamini, S.B.; Kumar, A. and Ateba, C.N. (2019). Antimicrobial resistance factors of extended-spectrum beta-lactamases producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from cattle farms and raw beef in North-West Province, South Africa. Biomedical Research International.
- Mostafavi, M.; Wang, L.; Xie, L.; Takeoka, K.T.; Richie, D.L.; Casey, F.; Ruzin, A.; Sawyer, W.S.; Rath, C.M. and Wei, J.R. (2018). Interplay of *Klebsiella pneumoniae* fabZ and lpxC Mutations Leads to LpxC Inhibitor-Dependent Growth Resulting from Loss of Membrane Homeostasis. mSphere.;3 doi: 10.1128/mSphere.00508-18.
- Moussé, W.; Adjanohoun, A.; Sina, H.; Noumavo, P.A.; Ahissin, D. and Baba-Moussa, L. (2016). *Klebsiella pneumoniae* isolated from street foods: characterization for extended-spectrum  $\beta$ -lactamases production and antibiotics resistance profile. Biotechnology and Applied Biochemistry, 4(2): 27-37.
- Nada, R.; Zainab, M.; Ameen, S. and Jinan, H. (2024). The Effect of Alcoholic, Aqueous, and Crude Extracts of Lemon Citrus Seeds on *Staphylococcus* and *Klebsiella* Bacteria. Research & Reviews: Journal of Microbiolo-

- gy and Virology, 14(3): 32–36.
- NCBI taxonomy Bethesda, M.D. (2019).** National Center for Biotechnology Information. Retrieved 24 April 2019.
- Nicole, C. and Panarelli, M.D. (2024).** Gastrointestinal and Liver Pathology (Third Edition) chapter (9) Infectious Diseases of the Gastrointestinal Tract A Volume in the Series: Foundations in Diagnostic Pathology Foundations in Diagnostic Pathology, Pages 243–298.
- Paczosa, M.K. and Mecsas, J. (2016).** *Klebsiella pneumoniae*: going on the offense with a strong defense. Microbiol. Microbiology and Molecular Biology Reviews 80, 629–661.
- Prajapati, B.R.; Parmar, B.C.; Bhandari, B.B.; Nayak, M.N.B.J.B. and Chaudhary, J.H. (2022).** Anti-Microbial Susceptibility Pattern of Extended Spectrum Beta-Lactamase (ESBL) Producing *Klebsiella* spp. Isolated from Chevron Marketed in Anand, Gujarat. The Indian Journal of Veterinary Sciences and Biotechnology, 18(2): 73.
- Pruss, A.; Wrona, M.; Kwiatkowski, P.; Masiuk, H.; Cettler, M.; Giedrys-Kalemba, S.; Dudzin´ska, E. and Dolegowska, B. (2023).** Virulence genes and antibiotic resistance among clinical *Klebsiella pneumoniae* strains. Pomeranian Journal of Life Sciences 69, 1–9.
- Ouattara, B. (1997).** Antibacterial activity of selected fatty acids and essential oils against six meat spoilage organisms. International Journal of Food Microbiology, 37: 155–162.
- Ramadan, M.; Soliman, E.A.; Abd El Tawab, A.A. and Elhofy, F.I. (2023).** Identification and characterization of *klebsiella pneumonia* isolated from farm animals and their biofilm production estimation Benha Veterinary Medical Journal 44: 70–73.
- Riwu, K.H.P.; Effendi, M.H.; Rantam, F.A.; Khairullah, A.R. and Widodo, A. (2022).** A review: Virulence factors of *Klebsiella pneumonia* as emerging infection on the food chain. Vet. World.;15(9).
- Rodrigues, C.; Hauser, K.; Cahill, N.; Li-gowska-Marzeta, M.; Centorotola, G. and Cornacchia, A. (2022).** High prevalence of *Klebsiella pneumoniae* in European food products: a multicentric study comparing culture and molecular detection methods. Microbiology Spectrum, 10(1): e02376–21.
- Sarowska, J.; Choroszy-Krol, I.; Jama-Kmiecik, A.; Maczyn´ska, B.; Cholewa, S. and Frej- Madrzak, M. (2022).** 1 Occurrence and characteristics of carbapenem-resistant *Klebsiella pneumoniae* strains isolated from hospitalized patients in Poland – A single centre study. Pathogens 11, 859.
- Saurel, O.; Iordanov, I.; Nars, G.; Demange, P.; Le Marchand, T.; Andreas, L.B.; Pintacuda, G. and Milon, A. (2017).** Local and Global Dynamics in *Klebsiella pneumoniae* Outer Membrane Protein a in Lipid Bilayers Probed at Atomic Resolution. J. Am. Chem. Soc. 2017;139:1590–1597. doi: 10.1021/jacs.6b11565.
- Schonborn, S.; N. Wente; J.H. Paduch and V. Kromker (2017).** In vitro ability of mastitis causing pathogens to form biofilms. J. Dairy Res. 84:198–201.
- Schroll, C.; Barken, K.B.; Krogfelt, K.A. and Struve, C. 2010 .** Role of type 1 and type 3 fimbriae in *Klebsiella pneumoniae* biofilm formation. BMC Microbiol. 10:179 doi: 10.1186/1471-2180-10-179.
- Shaik, G.; Sujatha, N. and Mehar, S.K. (2014).** Medicinal plants as source of antibacterial agents to counter *Klebsiella pneumoniae* Journal of Applied Pharmaceutical Science Vol. 4 (01), pp. 135–147.
- Sikkema, J. (1995).** Mechanisms of membrane toxicity of hydrocarbons. Microbiological Reviews, 59: 201–222.
- Sivaraman, G.K.; Rajan, V.; Vijayan, A.; Elangovan, R.; Prendiville, A. and Bachmann, T.T. (2021).** Antibiotic resistance profiles and molecular characteristics of extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from shrimp aquaculture farms in Kerala, India. Frontiers in Microbiology 12, 622891.
- Song, S.; He, W.; Yang, D.; Benmouffok, M.; Wang, Y.; Li, J.; Sun, C.; Song, X.; Ma, S.; Cai, C.; Ding, S.; Wu, C.; Shen, Z. and Wang, Y. (2022).** Molecular epidemiology of *Klebsiella pneumoniae* from clinical bovine mastitis in Northern Area of China, 2018–2019. Engineering 10, 146–154.
- Sugiyama, M.; Watanabe, M.; Sonobe, T.; Kibe, R.; Koyama, S. and Kataoka, Y. (2022).** Efficacy of antimicrobial therapy for

- bovine acute *Klebsiella pneumonia* mastitis. The Journal of Veterinary Medical Science 84, 1023–1028.
- Tekiner, İ.H. and Özpınar, H. (2016).** Occurrence and characteristics of extended-spectrum beta-lactamases-producing Enterobacteriaceae from foods of animal origin. Brazilian Journal of Microbiology, 47: 444–451.
- Theocharidi, N.A.; Balta, I.; Houhoula, D.; Tsantes, A.G.; Lalliotis, G.P. and Polydera, A.C. (2022).** High prevalence of *Klebsiella pneumoniae* in Greek meat products: detection of virulence and antimicrobial resistance genes by molecular techniques. Foods, 11(5): 708.
- Tian, F.; Li, Y.; Wang, Y.; Yu, B.; Song, J.; Ning, Q.; Jian, C. and Ni, M. (2023).** Risk factors and molecular epidemiology of fecal carriage of carbapenem resistant Enterobacteriaceae in patients with liver disease. Annals of Clinical Microbiology and Antimicrobials 22, 10.
- Voon, H.C.; Bhat, R. and Rusul, G. (2012).** Flower extracts and their essential oils as potential antimicrobial agents for food uses and pharmaceutical applications. Comprehensive Reviews in Food Science and Food Safety, 11( 1): 34–55, 2012.
- Wang, G.; Zhao, G.; Chao, X.; Xie, L. and Wang, H. (2020).** The characteristic of virulence, biofilm and antibiotic resistance of *Klebsiella pneumoniae*. Int. J. Env. Res. Pub. He. 17:6278.
- Wang, X.; Wang, Y.; Zhou, Y.; Li, J.; Yin, W. and Wang, S. (2018).** Emergence of a novel mobile colistin resistance gene, mcr-8, in NDM-producing *Klebsiella pneumoniae*. Emerging Microbes & Infections, 7(1): 1–9.
- Wareth, G. and Neubauer, H. (2021).** The animal-foods-environment interface of *Klebsiella pneumoniae* in Germany: an observational study on pathogenicity, resistance development and the current situation. Veterinary Research 52, 16.
- Wei, D.D.; Chen, K.Q. and Wang, L.H. (2016).** Clinical and molecular characteristics of high virulent *Klebsiella pneumonia* in infection in intensive care unit. Chin. J. Nosocomiol., 26(1): 5056–5059.
- World Health Organization (WHO) (2017).** <https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed>.
- Wu, X.; Liu, J.; Feng, J.; Shabbir, M.A.B.; Feng, Y.; Guo, R.; Zhou, M.; Hou, S.; Wang, G.; Hao, H.; Cheng, G. and Wang, Y. (2022).** Epidemiology, environmental risks, virulence, and resistance determinants of *Klebsiella pneumoniae* from dairy cows in Hubei, China. Frontiers in Microbiology 4, 858799.
- Yang, F.; Shen, C.; Zheng, X.; Liu, Y.; El-Sayed Ahmed, M.A.E.G. and Zhao, Z. (2019).** Plasmid-mediated colistin resistance gene mcr-1 in *Escherichia coli* and *Klebsiella pneumoniae* isolated from market retail fruits in Guangzhou, China. Infection and Drug Resistance, 385–389.
- Yang, Y.; Peng, Y.; Jiang, J.; Gong, Z.; Zhu, H.; Wang, K.; Zhou, Q.; Tian, Y.; Qin, A.; Yang, Z. and Shang, S. (2021).** Isolation and characterization of multidrug-resistant *Klebsiella pneumoniae* from raw cow milk in Jiangsu and Shandong provinces, China. Transboundary and Emerging Diseases 68, 1033–1039.
- Zhang, S.; Yang, G.; Ye, Q.; Wu, Q.; Zhang, J. and Huang, Y. (2018).** Phenotypic and genotypic characterization of *Klebsiella pneumoniae* isolated from retail foods in China. Frontiers in Microbiology, 9: 289.
- Zhao, W.H.; Hu, Z.Q.; Okubo, S.; Hara, Y. and Shimamura, T. (2001).** Mechanism of synergy between epigallocatechin gallate and beta-lactams against methicillin-resistant *Staphylococcus aureus*. Antimicrobial Agents and Chemotherapy, 45(6): 1737–1742.