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Synergistic effect of mannan extracted from *Saccharomyces cerevisiae* with antibiotics against multidrug resistant *Escherichia coli*

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Abstract:
Multidrug-resistant *Escherichia coli* (MDR-*E. coli*) presents a formidable healthcare challenge, continuously evolving resistance to conventional antibiotics. The aim of this study focuses on assessing the synergistic effect and enhance the effectiveness of traditional antibiotics of mannan extracted from *Saccharomyces cerevisiae* on MDR-*E. coli*. Clinical samples (n=150) were collected from several hospitals in Baghdad for both sexes between August and December 2022, including 73 urine, 10 catheter, 13 wound, and 54 stool samples. Among the total collected samples, 112 *E. coli* isolates were obtained, with 54 derived from urine, 9 from catheter samples, 6 from wound samples, and 43 from stool samples. Antimicrobial susceptibility test (AST) revealed resistance to imipenem (0%) and amikacin (2%), with sensitivity observed for cefotaxime (25%), gentamicin (29%), ceftriaxone (28%), ciprofloxacin (41%), norfloxacin (34%), trimethoprim-sulfamethoxazole (48%), and tetracycline (35%). Mannan purified from *S. cerevisiae* demonstrated inhibitory effects on *E. coli* growth, with Minimum Inhibitory Concentrations (MIC) ranging from 100 to 12.5 mg/mL and Minimum Bactericidal Concentrations (MBC) from 25 to 200 mg/mL. Furthermore, mannan exhibited a synergistic effect with conventional antibiotics, pointedly boosting the efficacy of gentamicin (250%), cefotaxime (160%), ceftriaxone (340%), ciprofloxacin (344.4%), norfloxacin (337.5%), and trimethoprim-sulfamethoxazole (237.5%). This research addresses the public health threat posed by MDR-*E. coli*, highlighting the potential of *S. cerevisiae* mannan as a promising solution for inhibiting *E. coli* and improving antibiotic efficacy.

Keywords: Antimicrobial Susceptibility Test, Combination effect, *E. coli*, Mannan, *Saccharomyces cerevisiae*.

1.Introduction:

Escherichia coli (*E. coli*), belonging to the Enterobacteriaceae family, is a significant component of the human and animal intestinal flora (*Leone and Ferrante*, 2023). Its prevalence, constituting approximately 0.1% of the intestinal flora, can vary based on factors such as geographical location, diet, medications, and travel, leading to dysbiosis. This variation is associated with various infections, including urinary tract infections, bacteraemia, pneumonia, septicaemia, and meningitis (*Bonten et al.*, 2021). *E. coli* employs enzymes and resistance mechanisms against antibiotics, making it highly resistant to conventional treatments (*Qian et al.*, 2020). Its ability to alter cell membrane permeability, target location, inhibit protein synthesis, and use efflux pumps further complicates therapeutic approaches (*Oudih and Harhara*, 2021).

Saccharomyces cerevisiae (*S. cerevisiae*) yeast has played an active role in humans' life and has gained great importance in the field of public health, food industry, animal feeding, and pharmaceutical manufacturing (*Faustino et al.*, 2021). One of the main reasons for this importance is the components of the yeast cell wall (YCW) which increase the concern of these components in the communication between cell to cell at the level of the yeast cells themselves and their effect as a stimulus or immunomodulatory activity for both human and animal (*Wang et al.*, 2022).

Mannan monosaccharide (MON) is an indigestible water-soluble component made from mannose residues linked by α-1,6 bonds with sub-strings consisting of α-1,2 and α-1,3 bonds (*Razan*, 2021). Mannan gained an advantage as it is a non-toxic substance and has no side effects on the health of the host. It owns the ability to prevent the adhesion of pathogenic bacteria by binding with these bacteria, adsorbing them, and controlling the disease (*Kango et al.*, 2022). Because the frequency and severity of infection with this bacterium represent an economic and psychological burden for those infected and huge losses for health institutions in general, it was necessary to search for treatment methods to reduce the number and spread of disease cases. This study aimed to examine the inhibitory impact of mannan on *E. coli* strains isolated from various pathological sources. Additionally, it assessed its influence on biofilm formation and its potential in enhancing the efficacy of conventional antibiotics utilized in the treatment of *E. coli* infections.

2.Materials and Methods

2.1.Samples collection and diagnosis

Samples were collected from August to December 2022 from Al-Elwiya Maternity Hospital, Ibn Al-Nafis Hospital, and Sheikh Zayed Hospital in Baghdad. These samples included 73 urine, 10 catheter, 13 wound, and 53 stool samples, totaling 150 from both male and female patients. *E. coli* isolates were cultured on MacConkey agar and EMB agar, and colonies were examined based on various characteristics after 24 hours of incubation at 37°C. Further, Gram staining and microscopic examination of isolates were performed. The VITEK®2 compact system, using GN Card ID, rapidly diagnosed the *E. coli* isolates from different clinical sources. The bacterial suspensions' turbidity was determined by the VITEK®2 DENSICHEK device, and results were recorded after approximately 4-6 hours in accordance with the instructions provided by BIOMÉRIEUX-France's.

2.2.Antibiotic susceptibility test (AST)

Following the guidelines set by the Clinical and Laboratory Standards Institute (CLSI M100 32th Edition 2022), the AST was conducted for *E. coli* using Kirby Bauer's disk diffusion method. Nine different commonly prescribed antibiotics were used: Amikacin 30µg, Gentamicin 10µg, Cefotaxime 30µg, Ceftriaxone 30µg, Ciprofloxacin 5µg, Norfloxacin 10µg, Trimethoprim-Sulfamethoxazole 1.25/23.75µg, Tetracycline 30µg, and Imipenem 10µg. Organisms displaying resistance to at least three antibiotics from various structural classes were classified as multidrug-resistant (MDR), following CLSI guidelines.

2.3.Mannan extraction

To extract mannan from *S. cerevisiae*, 5 grams of yeast were mixed with a 1% sodium hydroxide solution (50 mL) and heated at 100°C for two hours. Subsequently, the soluble mannan oligosaccharide was cooled, neutralized to a pH of 7 using a diluted HCl (10%) solution, and then precipitated by adding 200 mL of absolute ethanol. The mixture was filtered following the protocol established by Huang *et al.* (2010) and the resulting precipitate was washed with both diethyl ether and absolute ethanol. The filtrate was discarded and the precipitate taken to be dissolved in an appropriate amount of distilled water. At this stage was obtained crude mannan. To obtain deproteinized mannan, Trichloroacetic acid (TCA) at a 10% concentration was used to adjust the pH of crude mannan to 3, initiating a 24-hour incubation at 4°C. Subsequent steps involved centrifugation, ethanol precipitation, further

centrifugation, and sediment dissolution in distilled water, followed by a heating process at 121°C for three hours, based on the methodology outlined by Razan and Odongo (2020). More details about mannan extraction and purification can be consulted in (*Fadhil Abbas Al-Helli and Abdul Sattar Salman*, 2023).

2.4.Antibacterial activity of mannan against MDR-*E. coli* isolates

Mannan from *S. cerevisiae* was assessed for inhibitory activity in a 96-well microtiter plate. To find the MIC, each well was filled with sterile Mueller-Hinton broth (125 µL per well). Mannan solutions (concentration range: 200 to 3.125 mg/µL) were initially added to the first column and then serially transferred to the next wells, except the last column, maintaining 125 µL in each well. The positive control contained only Mueller-Hinton broth, and the negative control included a bacterial suspension. An *E. coli* bacterial suspension was created by diluting it 1:100 with Mueller-Hinton broth and added to wells with mannan and the positive control. The suspension's turbidity was adjusted to 0.5 McFarland, and the microtiter plate was covered and incubated at 37°C overnight. Following incubation, 30 µL of 0.015 Resazurin dye was added to all wells. The plate was further incubated for 1/2 to 3 hours at 37°C to check for a colour change, indicating dye reduction. The MIC was identified as the lowest mannan concentration preventing bacterial growth, with no dye reduction and colour change from dark blue to bright pink. A Mueller-Hinton agar plate was inoculated with a bacterial suspension exceeding the identified MIC. The Minimum Bactericidal Concentration (MBC) was defined as the lowest concentration where no bacterial colonies were observed to grow on the agar plate (*Wu et al.*, 2023).

2.5.Evaluation of the combined effect of antibiotics and mannan on MDR-*E. coli* isolated from different sources.

The antibiotics to which the *E. coli* showed resistance were selected for this assay. The synergistic impact of six antibiotics only (gentamycin, cefotaxime, ceftriaxone, ciprofloxacin, norfloxacin, and trimethoprim-sulfamethoxazole) in combination with mannan was investigated using an adapted approach based on a modified method by Roy *et al.* (2010). Mannan- submerged paper discs were placed on Mueller-Hinton agar plates with MDR-*E. coli*. After 24 hours of incubation at 37°C, inhibition zones were measured. Only antibiotics to which *E. coli* exhibited resistance were considered, and the study used antibiotic-alone inhibition diameters as a control. The percentage increase fold was calculated using the specified equation (Fold increase% = (b-a)/a×100) by Ghosh *et al.* (2012). Where (a) represents the inhibition zones

(mm) for an antibiotic alone, and (b) represents the inhibition zones (mm) for the antibiotic in combination with mannan.

3.Results and Discussion

3.1.Cultural and microscopic examination

Colony morphology was examined on MacConkey agar. Characteristics such as colour, size, and colony edges were noted following a 24-hour incubation at 37°C. Subsequently, positive isolates were validated by culturing them in Eosin-Methylene Blue (EMB) medium at 37°C for 24 hours. Identification was confirmed by the distinctive bright metallic green colour of the colonies on this medium. A single colony of each isolate was fixed on a clean slide to study gram stain under a light microscope (*Erjavec*, 2019). Out of the total number of samples (n=150) comprising 73 urine,10 catheter,13 wound and 54 stool samples, a total of 112 isolates were carried out in the following order: 54 isolates from urine samples, 9 isolates from catheter samples, 6 isolates from wound samples, and 43 isolates from stool samples. Table (1) shows the proportions of isolates according to the type of total samples and the sources of their isolation.

Table (1): E. coli isolates isolated from different clinical sources

Samples	No. of Samples	No. of isolates	Percentage of isolates according total samples	Percentage of isolates according samples source
Urine	73	54	36.0%	73.9%
Stool	54	43	28.61%	79.6%
Wound	13	6	4.0%	46.1%
Catheter	10	9	6.0%	90.0%

E. coli is the main cause of urinary tract infections (UTIs). It possesses specific virulence genes, including the (fem) gene for type one pili production and Fim H adhesin for invading bladder cells (*Pokharel et al.*, 2023). P-fimbria adhesins attach to uro-epithelial cells, and UPEC carries the (Sfa/Dr family) fimbria of antigens that enhance colonization, increasing the risk of recurring UTIs. This feature is more common in UPEC than in *E. coli* causing diarrhea (*Radera et al.*, 2023). *E. coli* causes catheter-associated UTIs by colonizing the intestinal and urinary tracts. Catheter insertion introduces opportunistic organisms, increasing susceptibility. Flagella help *E. coli* ascend from the catheter to the bladder. Catheter material affects colonization and biofilm formation (*Sanchez et al.*, 2022). *E. coli* isolates from various wound types exhibit distinct virulent factors compared to other strains. These factors encompass a heightened prevalence of aerobactin

synthesis and uptake, a unique resistance pattern observed in bacterial isolates from burn wounds in an Iraqi hospital as stated by Tayh *et al.* (2023) , α-hemolysin, cytotoxic necrotizing factor, and S-fimbriae. The genes encoding these factors are situated on pathogenicity islands (PAI) (*Ssekatawa et al.*, 2020). While this bacterium can remain asymptomatic, under favorable conditions, they utilize these virulence factors to infiltrate extra-intestinal areas in susceptible hosts (*Longhi et al.*, 2022). Finally, *E. coli* isolates from stool samples differ based on the genes responsible for encoding them (*Abdulqader et al.*, 2022). Cytotoxic Necrotizing Factor 1,2 genes are found in enterotoxigenic *E. coli* (*Jarquin et al.*, 2022). While Bundle-forming Pilus (bfpA) and Enteropathogenic Attachment and Effacement (eaeA) genes are responsible for encoding Enteropathogenic *E. coli* (EPEC) (*Maniha and Noor*, 2020). Additionally, Heat-stable and Heat-labile toxin genes are responsible for encoding Enterotoxigenic *E. coli* and Shiga-like toxin (Stx1) and (Stx2) genes are responsible for encoding Shiga-like toxin-producing *E. coli* (STEC) (*Huang et al.*, 2021).

3.2. Antibiotic susceptibility test results

The results of the antibiotic susceptibility test were interpreted according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) (*Jacobs et al.*, 2022). Antibiotic susceptibility tests are crucial for evaluating effectiveness against *E. coli* infections. *E. coli* strains classified as Multidrug Resistant (MDR) are resistant to three or more antimicrobial agents, posing a significant public health risk (*Rafailidis and Kofteridis*, 2022). Imipenem, introduced to the market in 1987, is a potent inhibitor of a wide range of Gram-positive and Gram-negative bacteria (*Zhanel et al.*, 1998). However, resistance to imipenem has been recorded in various parts of the world (*Karikari et al.*, 2022). *E. coli* resistance to aminoglycosides is mainly attributed to the production of aminoglycoside-modifying enzymes (AMEs) (*Pradier and Bedhomme*, 2023).

The AST results in this study showed that, imipenem (0%) and amikacin (1%), with sensitivity observed for cefotaxime (25%), gentamicin (29%), ceftriaxone (28%), ciprofloxacin (41%), norfloxacin (34%), trimethoprim-sulfamethoxazole (48%), and tetracycline (35%). The results of AST are summarized in Figure (1).

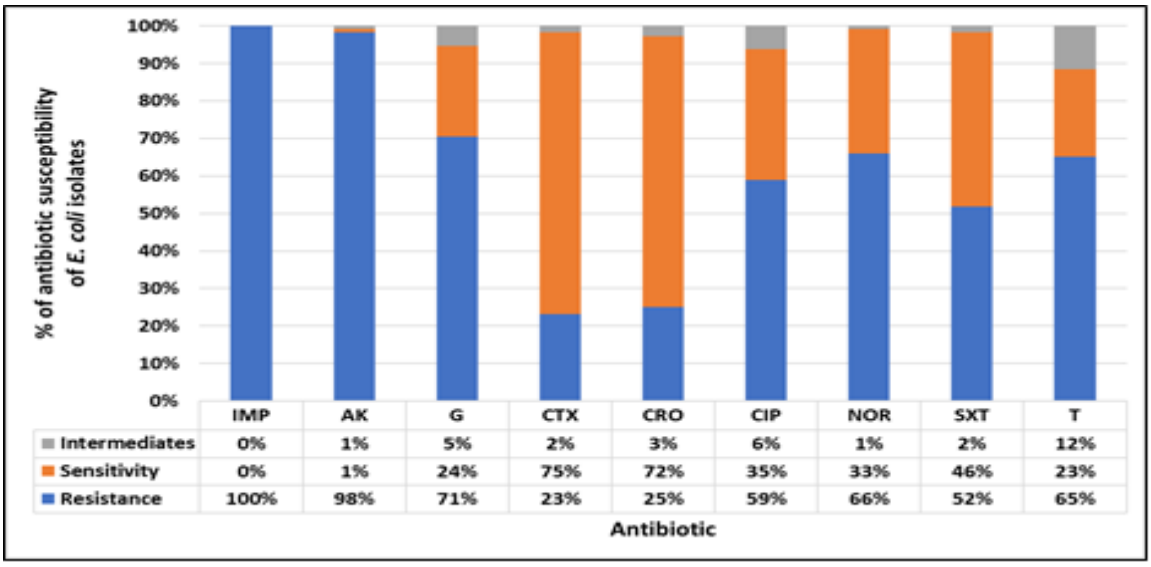

Figure (1): Percentage of AST results of *E. coli* isolates (n=112)

The percentage of resistance to gentamicin in this study closely aligned with the rate reported by Wu *et al.* (2021). Plasmid-mediated quinolone resistance (PMQR) determinants may significantly contribute to bacterial survival in the presence of quinolones. Another resistance mechanism involves the physical blocking of target sites by (Qnr) proteins or the increased expression of efflux pumps to expel antibiotic molecules (*van Driel et al.*, 2019). *E. coli* develops resistant to cephalosporins upon acquiring Expanded Spectrum Beta-Lactamases (ESBLs) such as TEM-1, TEM-2, and SHV-1 (*Yasir et al.*, 2020), or it may be linked to the production of plasmidic class C β-lactamases, such as the CMY enzyme (*Judge et al.*, 2023). Often, trimethoprim and sulfamethoxazole are used together in various quantities depending on the target bacteria, providing synergistic bactericidal activity (*Kawahara et al.*, 2023). Changes to the permeability of the cell wall and excessive production of dihydrofolate reductase, either through chromosomal mutations or plasmid-mediated acquisition of trimethoprim-resistant DHFR enzymes (dfr) genes (*Saito et al.*, 2022). Despite the decline in the use of tetracycline in humans and animals, resistance to tetracycline continues to increase. The main reason for this increase is the spread of (tet) genes among bacteria due to the continued use of tetracyclines in animal production worldwide (*Çiçek et al.*, 2022).

3.3. Extraction of mannan oligosaccharide

The final yielded dry weight of mannan extraction amounted to 37.6 g/L. The extraction procedure comprised subsequent phases: solvent penetration into the solid components, solute dissolution in the solvent, and solvent diffusion out of the solid matrix (*Sayakulu and Soloi*, 2022). NaOH is commonly employed in extraction procedures due to its affordability, ease of use, and effectiveness in producing optimal alkaline solutions for treating natural fibres (*Zhang et al.*, 2018). It was observed that mannan and surface proteins within the yeast wall exhibit a spontaneous binding tendency at specific pH levels. Additionally, molecular study's findings revealed that the surface proteins had varying binding sites for mannan, dependent on pH, mainly influenced by hydrogen bonds and hydrophobic interactions. These findings affirm that the interaction between surface proteins and mannan at pH 5.0 demonstrates enhanced binding affinity and greater structural stability (*Fu et al.*, 2023).

3.4. Antibacterial activity of mannan against *E. coli* isolates from different source

The results of MIC and MBC of *E. coli* isolates are defined in Table (2). Mannan, a complex carbohydrate composed of mannose units, affects the growth of *E. coli* depending on its concentration and type. At low concentrations, mannan promotes growth by acting as a carbon source for the bacteria. *E. coli* breaks down mannan into smaller sugars and metabolizes them through the glycolytic pathway (*Scribano et al.*, 2020). However, at high concentrations, mannan inhibits growth by forming a viscous gel that limits bacterial motility and cell division. The viscosity of the mannan solution can also restrict nutrient uptake, leading to growth inhibition (*Wagenlehner et al.*, 2022). The effect of mannan on the growth of *E. coli* is that it increases the production of oxygen free radicals inside the bacterial cell, which kills the bacteria (*Smith et al.*, 2022). This physiological change is characterized by greater peptide abundance of key TCA proteins in response to ROS overproduction in the presence of mannan in the culture medium. Additionally, mannan may contribute to hyperactivity of the electron transport chain. The MIC of mannan on *E. coli* may vary depending on the source of bacterial isolates and mannan source (*Smith et al.*, 2020).

Table (2): MIC and MBC results of mannan against *E. coli*.

Bacterial isolates	MIC mg/mL	MBC mg/mL
E. coli **(C1)**	50	100
E. coli **(C2)**	50	100
E. coli **(C3)**	12.5	25
E. coli **(W4)**	50	100
E. coli **(W5)**	100	200
E. coli **(W6)**	50	100
E. coli **(U7)**	100	200
E. coli **(U8)**	100	200
E. coli **(U9)**	50	100
E. coli **(S10)**	100	200
E. coli **(S11)**	100	200
E. coli **(S12)**	50	100

C= isolate from catheter, W= isolate from wound, U= isolate from urine, S= isolate from stool

3.5. Evaluation of combined effect between antibiotics and mannan on *E. coli* isolates

The results of studying the synergistic effects of antibiotics combined with mannan from *S. cerevisiae* against MDR-*E. coli* isolates were recorded and analysed, as illustrated in Table 3.

Table (3): Combination effect of mannan with antibiotics on MDR-*E. coli* isolates from different sources

No. of isolate	Inhibition zone in (mm)																	
	G			CTX			CRO			Cip			Nor			SXT		
	a	b	%	a	b	%	a	b	%	a	b	%	a	b	%	a	b	%
E. coli **(C1)**	-	-	-	10	24	**140**	10	30	**200**	9	35	**288.8**	15	36	**140**	8	27	**237.5**
E. coli **(C2)**	9	24	**166.6**	-	-	-	-	-	-	10	20	**100**	9	18	**100**	8	21	**162.5**
E. coli **(C3)**	10	35	**250**	10	26	**160**	15	26	**73.3**	9	40	**344.4**	8	35	**337.5**	-	-	-

E. coli **(W4)**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E. coli **(W5)**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E. coli **(W6)**	8	18	**125**	9	17	**88.8**	10	23	**130**	9	31	**244.4**	8	29	**262.5**	-	-	-
E. coli **(U7)**	10	24	**140**	9	21	**133.3**	5	22	**340**	10	30	**200**	15	29	**93.3**	-	-	-
E. coli **(U8)**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E. coli **(U9)**	4	10	**150**	9	11	**22.2**	9	14	**55.5**	-	-	-	-	-	-	10	12	**20**
E. coli **(S10)**	9	16	**77.7**	10	15	**50**	8	19	**137.5**	12	15	**25**	8	15	**87.5**	10	12	**207**
E. coli **(S11)**	7	10	**42.8**	6	12	**100**	10	12	**20**	9	11	**22.2**	5	9	**80**	4	10	**150**
E. coli **(S12)**	10	12	**20**	12	15	**25**	8	11	**37.5**	9	15	**66.6**	10	13	**30**	-	-	-

a: diameter zone of inhibition for antibiotic alone, **b:** diameter zone for inhibition of antibiotic for mannan with antibiotic, **%:** percentage of increasing fold zone diameter, **C:** catheter, **W:** wound, **U:** urine, **S:** stool. **(-):** not tested because sensitive for particular antibiotic. **G:** gentamycin, **CTX:** cefotaxime, **CRO:** ceftriaxone, **Cip:** ciprofloxacin, **Nor:** norfloxacin, **SXT:** trimethoprim-sulfamethoxazole.

The results revealed variations in the diameters of inhibition zones around antibiotic discs when used alone compared to when impregnated with mannan. The observed differences were recorded the highest antibacterial effect by mannan and gentamycin (G) showing equal 250% in the inhibition zone of *E. coli* (C3), while lowest effect was 20% in the inhibition zone of *E. coli* (S12). For mannan and cefotaxime (CTX) combination, the highest fold increase of 160% in the inhibition zone of *E. coli* (C3), while lowest effect was 22.2% in the inhibition zone of *E. coli* (U9). The highest antibacterial effect 340% in the inhibition zone of *E. coli* (U7) by mannan and ceftriaxone (CRO) while lowest effect was 20% in the inhibition zone of *E. coli* (S11). For mannan and ciprofloxacin (Cip) combination, the highest fold increase of 344.4% in the inhibition zone of *E. coli* (C3), while lowest effect was 22.2% in the inhibition zone of *E. coli* (S11). The highest antibacterial effect 337.5% in the inhibition zone of *E. coli* (C3) by mannan and norfloxacin (Nor) while lowest effect was 30% in the inhibition zone of *E. coli* (S12). Finaly For mannan and trimethoprim-sulfamethoxazole (SXT) combination, the highest fold increase of 237.5% in the inhibition zone of *E. coli* (C1), while lowest effect was 20% in the inhibition zone of *E. coli* (U9).

Usage of a single treatment is frequently ineffective because of factors such as drug resistance, constrained drug absorption, or challenges in reaching the intended site. To challenge these issues, combination therapy, involving the use of two or more drugs or a drug in combination with polymeric compounds, can be utilized (*Pena et al.*, 2021). This approach can help delay the development of resistance or control existing resistance, as it targets multiple pathways or mechanisms of action. By using a combination therapy approach, a lower dose of each drug can be employed, reducing toxicity and minimize side effects. The use of combination therapy has shown promise in improving treatment outcomes for a range of diseases and conditions (*Masri et al.*, 2019). An explanation for the impact of oligosaccharides on *E. coli* is linked to osmolarity. *E. coli* can react to changes in osmotic pressure induced by mannan, thereby enhancing antibiotic activity against *E. coli*(*Asadpoor et al.*, 2021). Another reason for the increased sensitivity of *E. coli* to the mannan-related antagonist is the multiple ionic interactions between the charged sugars and the surface of *E. coli*. This stimulates its negative charge on the surface of the *E. coli*, weakening its movement and agglomeration, and making it more sensitive to the antibiotic (*Powell et al.*, 2014). Although mannan may not inherently have antimicrobial properties, when administered alongside conventional drugs, it can enhance their effectiveness. The

therapeutic potential of this biopolymer's interaction with bacteria is influenced by various factors, including hydrophobicity, electrostatic attraction, van der Waals forces, and receptor-ligand interactions (*Masri et al.*, 2019).

4.Conclusion

In conclusion, the utilization of mannan extracted from yeast demonstrates significant potential in inhibiting the growth of *E. coli* and, when combined with traditional antibiotics, exhibits a powerful synergistic effect in the treatment of *E. coli* infections. This approach holds promise for addressing the challenges posed by antibiotic-resistant *E. coli* strains, offering a more effective and comprehensive strategy to combat this pathogen. However, further research and clinical trials are imperative to validate its safety, efficacy, and long-term implications for a promising addition to the treatments against *E. coli* infections.

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التأثير التآزري للمانان المستخلص من خميرة *Saccharomyces cerevisiae* مع المضادات الحيوية تجاه بكتريا *Escherichia coli* ذات المقاومة المتعددة

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مستخلص البحث:
تمثل الإشريكية القولونية المقاومة للأدوية المتعددة (MDR-*E. coli*) تحديًا هائلاً في مجال الرعاية الصحية، حيث تطور باستمرار مقاومتها للمضادات الحيوية التقليدية. الهدف من هذه الدراسة هو التركيز على تقييم التأثير التآزري وتعزيز فعالية المضادات الحيوية التقليدية للمانن المستخلص من خميرة *Saccharomyces cerevisiae* على MDR-*E. coli*. تم جمع العينات السريرية (العدد = 150) من عدة مستشفيات في بغداد لكلا الجنسين بين شهري آب وكانون الأول 2022، تضمنت 73 عينة بول، 10 قسطرة، 13 عينة جرح، و54 عينة براز. ومن بين إجمالي العينات التي تم جمعها، تم الحصول على 112 عزلة من الإشريكية القولونية، منها 54 عزلة من البول، و9 من عينات القسطرة، و6 من عينات الجروح، و43 من عينات البراز. أظهر اختبار الحساسية للمضادات الميكروبية (AST) وجود مقاومة للإيميبينيم (0%) والأميكاسين (2%)، مع ملاحظة حساسية للسيفوتاكسيم (25%)، والجنتاميسين (29%)، والسيفترياكسون (28%)، والسيبروفلوكساسين (41%)، والنورفلوكساسين. (34%)، تريميثوبريم-سلفاميثوكسازول (48%)، وتتراسيكلين (35%). أظهر المانن المنقى من S. cerevisiae تأثيرات مثبطة على نمو الإشريكية القولونية، حيث تراوح الحد الأدنى للتركيزات المثبطة (MIC) من 100 إلى 12.5 ملجم / مل والحد الأدنى لـ (MBC) من 25 إلى 200 ملجم / مل. علاوة على ذلك، أظهر المانن تأثيرًا تآزريًا مع المضادات الحيوية التقليدية، مما أدى إلى زيادة كبيرة في فعالية الجنتاميسين (250%)، سيفوتاكسيم (160%)، سيفترياكسون (340%)، سيبروفلوكساسين (344.4%)، نورفلوكساسين (337.5%)، وتريميثوبريم-سلفاميثوكسازول. (237.5%). يتناول هذا البحث التهديد على الصحة العامة الذي تشكله MDR-*E. coli*، حيث يعرض المانان المستخلص من خميرة الخبز عن حل واعد لتثبيط الإشريكية القولونية وتحسين فعالية المضادات الحيوية.

الكلمات المفتاحية: AST, Combination effect, *E. coli*, Mannan, *Saccharomyces cerevisiae*.