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Evaluated of the antibacterial activity of Fungal-Derived Taxol against pathogen isolated from cancer patients

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Abstract

Taxol production from Fusarium solani and its antibacterial evaluation against multidrug-resistant bacteria isolated from cancer patients. .this activity tested against them. . It including isolated and identification bacterial species from cancer patients and testes the fungal taxol on it by well diffusion method. Results show Staphylococcus aureus. with isolates 5, (5.5%) followed by S. haemolyticus (4, 4%), Escherichia coli (3, 3%), S. equorum, S. hyicus, and Enterococcus spp with (1,1%) for each. and the effect of extracted crud taxol on two types of bacteria (G+, G-), results show the significant effect of taxol on S. aureus (G+). more than E. coli (G-) tested the fungal Taxol in case of crud taxol while it no significant effect in any concentration (33%,66%,10%,50%)

Key words - bacterial pathogens, Cancer, bacteremia, bacteria coinfection

Introduction

Unquestionably, patients in oncology the districts are especially vulnerable to infections. These patients are more susceptible to infection due to cancer and chemotherapy. [1]. Cancer patients frequently contract infections, which can disrupt their treatment plan, result in longer hospital stays, raise medical expenses, and lower their chances of survival.

Infection is still a major or related cause of death, despite the fact that mortality rates have declined recently.. Bacteria are the most common cause of infection-associated mortality, followed by fungi. [2,3,4,5]. Finding new bioactive products is crucial right now because the medications used to treat various illnesses are expensive and have negative side effects [6,7].

The Pacific yew tree (Taxus spp.) is the original source of taxol, a highly functionalized anticancer medication that was the first billion-dollar drug in history. Due to the growing demand and scarcity of yew trees, very little taxol is produced by Taxus spp. Over the past two decades, there has been a lot of interest in identifying endophytic fungi that produce taxol from sources other than Taxus trees in order to meet production needs [8,9,10].

In 1993, the bioactive substance paclitaxel, also known as taxol, was identified in the endophytic fungus Taxomyces andreanae. The detection of taxol from various endophytic fungi was also investigated [11], and the process of separating endophytic fungi from plants is relatively straightforward. Furthermore, the taxol biosynthesis enzyme gene, dbat (encoding 10-deacetylbaccatin III-10-O-acetyltransferase), has been employed as a molecular marker for the purpose of identifying endophytic fungi that produce taxol [12,13]. Therefore, the purpose of the current study is to evaluate the prevalent infection types among cancer patients undergoing various forms of treatment. the bacterial pathogens that are associated with these infections, It also assessed the effectiveness of fungal taxol that was extracted from *Fusarium solani* against these associated bacteria.

2-Material and Methods

Taxol extraction and purification

In previous study, taxol produced from the *Fusarium solani* isolate identified and registered in the gene bank under the number PQ555253.1 was extracted and purified utilizing the method outlined by [14].

Collection and identification

Clinical specimens (blood specimens) from suspected infections (various cancers, period from May to October 2024) Specimens were transferred to the bacteriology lab in the hospital after put it in a suitable container and were **cultured on plates contain** MacConkey agar, blood agar, and chocolate agar. (Hi Media) and **they were incubated** for 18 hours at 35°C in an aerobic environment. after being stained with Gram stain. Antibiotic and biochemical tests have been validated using the Vitek 2

device. Using program version 7.01 and the AST-N201, AST-P632, ASTP586 and AST-ST01 cards for Gram negative bacteria, staphylococci, enterococci, and streptococci, respectively, we performed AST with the VITEK 2 system in compliance with the manufacturer's instructions.

Antimicrobial activity

The antimicrobial properties of crud fungal taxol were tested using the Agar wells diffusion method [15]. Gram-negative bacteria (*Escherichia coli*) and Gram-positive bacterial cultures (*Staphylococcus haemolyticus*) were used in this test

Statistical analysis

For statistical analysis, one-way ANOVA was employed with SPSS statistical software, version 20.0. Each experiment was carried out three times, and the results are shown as mean ± standard deviation (SD).

Results and discussion

Taxol extraction

Figure (1) show the scheme of extraction Taxol that used in this study

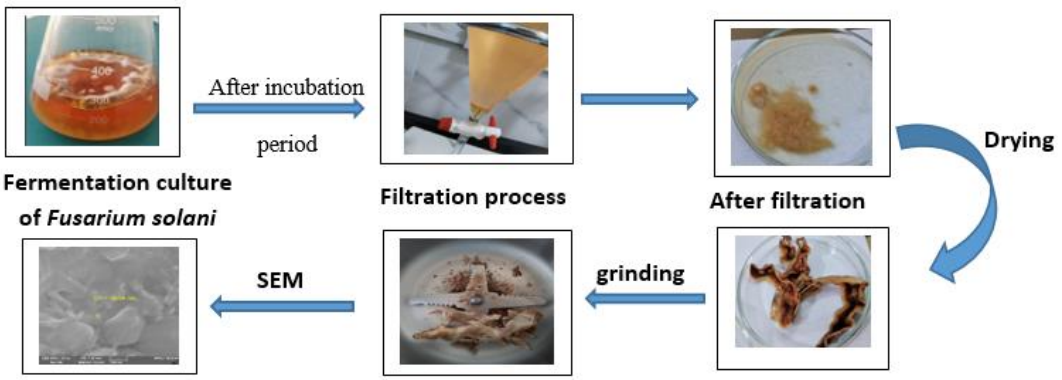

Figure (1) the scheme of extraction Taxol

Collection and identification

Prevalence of microorganisms in samples: 17 of 100 samples had a significant bacterial population. Table 1.

Table 1: Distribution of the Sample

No. of specimens		%
growth	17	17%
No growth	83	83%
total	100	100%

In order to start the disease processes, pathogenic bacteria have a wide range of molecules and mechanisms that function as virulence factors and evade the host defenses. Bacteria secrete a variety of substances, including enzymes, toxins, and exopolysaccharides, in addition to their cell surface structures and metabolic arrangements. Numerous biomolecules have the ability to enter host cells. and have the ability to alter or destroy intracellular signaling and structures. [16]. In the end, each of these bacterial biomolecules increases virulence and could make clinical treatment more difficult. Autopsy studies show that about 60% of deaths in cancer patients with underlying hematological malignancies are caused by infectious complications, which are a major cause of morbidity and mortality in these patients. [17].

Figure (2) show number of specimens and type of cancer. Its appear among all cancer types, breast cancer is the one that is diagnosed the most frequently with (33, 33%) Uterus cancer with (29, 29%).And lung cancer with (23, 23%), Prostate cancer with (14,14%). Finally, Skin cancer with (2, 2%).In study by [18]. reported that The most common cancer diagnosed in women is breast cancer. It is the primary cause of cancer death for Black and Hispanic women, but it is the second most frequent reason for cancer-related deaths for women in general, after lung cancer. Breast cancer is one of the most common cancers for several reasons. Genetic Factors can play a role in increasing the risk of breast cancer, especially if there is a family history of the disease, Hormonal changes in the body, such as changes in estrogen and progesterone levels, can affect the risk of breast cancer, a few aspects of lifestyle, such as an unhealthy diet and lack of physical activity, can participate to an increased risk of breast cancer. Some environmental factors, such as exposure to radiation, can affect the risk of breast cancer. [18,19,20].

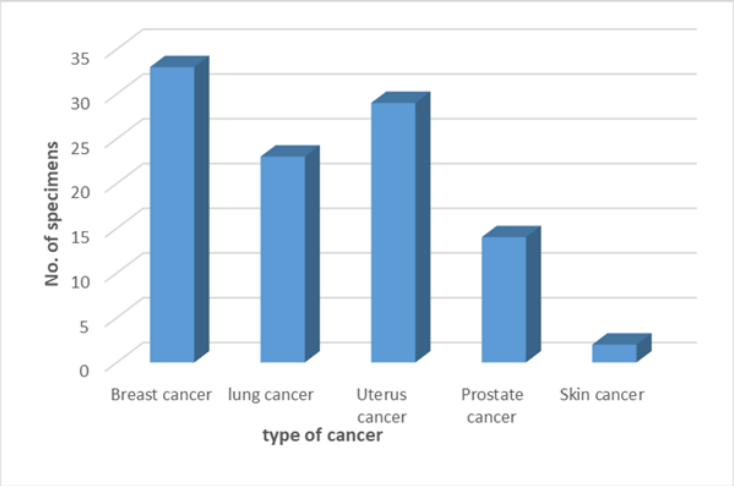

Figure (2) show number of specimens and type of cancer

The results of isolation and Identification by VITEK-2 System showed, Staphylococcus aureus. with isolates 5, (5.5%) followed by S. haemolyticus (4, 4%), Escherichia coli (3, 3%), S. equorum, S. hyicus, and Enterococcus spp with (1,1%) for each.

According to a study by Kumar *et al*. [21]. in Mumbai, the most prevalent pathogens were Pseudomonas species (26.2%), Enterococcus species (11.66%), S. aureus species (11.44%), E. coli species (11.34%), Klebsiella species (10.59%), and Acinetobacter species (9.95%) In our study, this was not the case, the cause may be in size of samples and environmental conditions.

Table (1) No. of isolates and percentage

genus	No. of isolates	%
Enterococcus spp	1	5.9
Escherichia coli	3	17.6
Klebsiella spp	2	11.8
Staphylococcus aureus	5	29.4
***S**. equorum*	1	5.9
S. haemolyticus	4	23.5
S. hyicus	1	5.9
Total no. (%)	17	100

Similar to the results of our investigation, another study reported that Gram-negative isolates accounted for 68.18% of bloodstream infection isolates. [22]. It was unclear whether cancer patients were at risk for bacterial infections. Immune-related side effects that necessitate immunosuppressive treatment may influence the risk of infection. [23].

The connection between some bacterial virulence factors and carcinogenesis is an interesting feature. It is believed that E. coli-induced

chronic inflammation in inflammatory bowel disease may increase the risk of colon cancer development. [24].

Antibacterial of extracted Taxol

The agar well diffusion method was used to assess fungal Taxol's antibacterial activity against bacterial pathogens. Figure (3), (4), appear effect of extracted crud taxol on two types of bacteria (G+, G-), results show the significant effect of taxol on S. aureus (G+). more than E. coli (G-)

This could be because many natural antimicrobials, like some fungal metabolites, tend to work better against Gram-positive bacteria than Gram-negative ones. In antimicrobial research, this is a typical pattern that Taxol occasionally follows. The two bacterial types' different cell envelope structures are the main cause of this effect.

Taxol, which has been isolated from a variety of fungal species, particularly endophytic fungi, has been shown in numerous studies to have antibacterial properties such as [25]. which discover that the fungal taxol have antibiotic-like effects on S. aureus, E. coli, and S. typhi. According to [26]. the antimicrobial activity of fungal taxol was assessed against two gram-positive bacterial strains, Bacillus subtilis (ATCC6633) and Staphylococcus aureus (ATCC12600), as well as a gram-negative bacterial strain, Escherichia coli (ATCC 25922).

Compared to its well-established mechanism in eukaryotic cancer cells, the mechanism of Taxol's effect on bacteria is still being studied and is not as well understood. The main cause of this is that bacteria do not have the intricate microtubule cytoskeleton that eukaryotic cells' Taxol targets. the mechanisms that have been suggested and examined: [27,28].
1 -FtsZ Interaction (The Leading Hypothesis): Bacterial "Tubulin": FtsZ (Filamenting temperature-sensitive mutant Z) is a protein found in bacteria that is thought to be a structural and functional homolog of eukaryotic tubulin. An essential part of the bacterial cell division apparatus is FtsZ.

Given that FtsZ and tubulin share structural similarities, it is hypothesized that Taxol may interact with FtsZ in a manner akin to that of tubulin. In the end, this interaction prevents the growth and proliferation of bacteria.
-Role in Cell Division: FtsZ polymerizes to create the Z-ring, a ring-like structure, at the mid-cell during bacterial cell division. The mother cell

eventually divides into two daughter cells as a result of this Z-ring constricting and a septum forming.

Although more conclusive proof and thorough mechanistic understanding are still required, some research has investigated the direct interaction between Taxol and FtsZ. If verified, focusing on FtsZ is a very alluring approach to creating novel antibiotics because it is crucial for bacterial survival and is mostly lacking in human cells, which may lessen off-target toxicity.

2- Membrane Disruption: The molecule taxol is comparatively lipophilic, or fond of fat. It can interact with and possibly insert itself into biological membranes, like bacterial cell membranes, due to this property. Increased permeability could result from such interaction, which would compromise the integrity of the bacterial cell membrane.

leakage of vital intracellular elements, such as proteins, ions, ATP, and nucleic acids. membrane potential loss .and Cell death may eventually result from this disturbance.

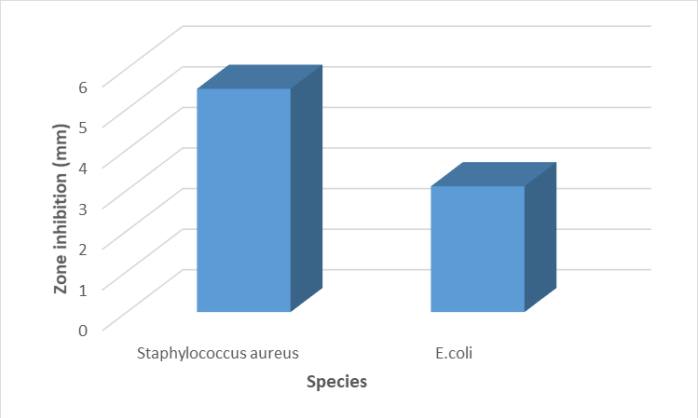

Figure (3), Effect of crude fungal taxol (100%)on isolated bacteria

	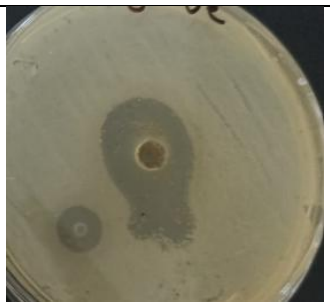
Staphylococcus aureus	*E.coli*

Figure (4)Inhibition effect of crude fungal taxol

Because we must present scientific facts in order to maintain the integrity of science. Since the current study looked at the effects of different dilutions of the taxol substance that was extracted from the fungus, it should be noted that no apparent inhibition was observed (Figure 5). This might be because, in addition to the bacteria's natural defense mechanisms, which are more effective when dealing with low concentrations of the compound, the concentration did not reach a concentration high enough to cause damage that the bacteria could not repair or overcome.

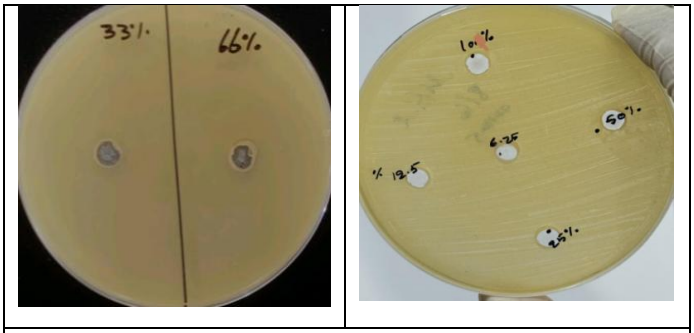

Figure (5).effect of different concentration of extracted Taxol on bacteria spp.

Conclusion

Numerous bacteria are connected in various ways to the development of cancer. Furthermore, the exact roles of various virulence factors and the complex interactions between particular bacteria and the target cells of our body are largely unknown. On the other hand, several microbial products are being investigated for potential use as therapeutic agents that fight cancer. Clinicians should always be careful to get patients to take part in screening tests while research is ongoing, especially if they are at risk for high-virulence pathogens. Cancer treatment can be enhanced by getting rid of these pathogens early in the course of the illness. The overall prognosis and survival of cancer patients are significantly impacted by secondary bacterial infections because of the immunosuppressive nature of cancer and the associated chemotherapy and radiation treatments.

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