The effect of UV radiation on O-7 Actinomycete in producing bioactive compounds in different growth conditions

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Abstract

Actinomycetes have been identified as an origin of many secondary metabolites, antibiotics and active components that impact microbial growth. Mediated mutations using UV in practice for the breeding of organisms. The objective of this study is to analyses the impact of UV radiation on the (O-7) Actinomycete isolate. This was a prospective analytical study of a severa of actinomycetes. The isolates were screened for antimicrobial efficacy against multiple Gram-positive, Gram-negative bacteria, yeast, and fungi. Various factors such as UV, temperature, pH, light, agitation, fermentation durations and aeration have also been boosted for optimal antimicrobial production. The isolate (O-7) Actinomycete has been recognized as a highly bioactive producing organism. The isolate was exposed to various wavelengths, times under numerous growth conditions. It was found that 4% concentration of glucose as a carbon source is significantly optimal for the production of antibiotic for (O-7) UV exposed strain, however, concentration of 1% of lactose is significantly optimal for the production of antibiotic for (O-7) UV exposed strain. Yeast extract at a concentration of 1% was found to be the best source of nitrogen for (O-7) UV exposed, while pH 7.0 was found to be the most suitable for the same isolate. From the temperature optimization study, it was observed that (O-7) exposed strain showed good growth and maximum antibiotic production at 28°C. The soil-isolated biological compounds (O-7) were effective against certain types of bacteria and fungi, and the research also demonstrated that exposure to UV radiation enhanced the production of these compounds.

1. Introduction

The Actinomycetes are responsible for the production of approximately half of the bioactive secondary metabolites found, antibiotics, anticancer agents, immunosuppressive agents, and enzymes (Law et al, 2020). In fact, 70–80% of available secondary metabolites were isolated and characterized from many actinomycetes species (Khanna et al., 2011).

Mutation is a permanent alteration of one or more nucleotides along the DNA strand at a specific site. Induced mutagenesis is commonly used to select microorganisms that produce biologically active compounds and to improve their activities (Alireza, 2016). The strain containing the mutation is called a mutant strain. The obstacle is to isolate the strains that are true mutants and carry beneficial mutations (Hu et al., 2001). Mutagenesis is the most reliable and commonly utilized tool for improving strain (Tao et al., 2019). Mediated mutations using UV rays, x-rays, y-rays, lasers, neutrons, and chemophoresis are practiced for microbe breeding (Yu et al, 1998). The most essential and efficient physical method for obtaining broad-spectrum mutations is UV radiation. It is secured to use UV light as a mutagen when compared to chemical mutagenesis (Demain and Adrio, 2008). Most Streptomyces groups are genetically unstable, and morphologically steady mutants are required for strain improvement strategies (Adrio et al., 2006).

The purpose of this study was to evaluate the effect of UV radiation on (O-7) Actinomycete in producing bioactive compounds in different growth conditions.

2. Material and Methods:

This was a prospective analytical study of a number of actinomycetes. Samples were separated from soils gained from many locations in Khartoum. The Crowded Plate method has been used...
to separate actinomycetes utilizing a set of media. The isolates were examined for antimicrobial efficacy against multiple Gram-positive, Gram-negative bacteria, yeast, and fungi. Multiple fermentation factors such as UV, temperature, pH, light, agitation, fermentation periods and aeration have been improved for optimal antimicrobial production. The strain (O-7) Actinomycetes has been described as a highly bioactive producing organism. The isolate was exposed to various UV wavelengths, times under multiple growth conditions.

2.1. Improvement of the strain

The UV mutagenesis method for the production of hyperantimicrobial stable UV mutants was applied to the selected soil isolate (O-7). The isolated Actinomycete (O-7) was spread over the surface of the actinomycete agar plates. The plates were then exposed to UV radiation at 254 nm and 324 nm at a distance of 25 cm for 5, 10, 15, 30, 60, 90, 120, 150, 180 s and more and then incubated at 27 °C for 24 h (Ray et al., 1994, Butler et al., 2003).

2.2. Stable mutant isolation

Stable mutants were grown in the broth medium and compared to the maximum antibiotic production by the cup-plate method. (Farekh et al., 2000, Okamoto et al., 2003). Morphological and cultural characteristics of the exposed strain (O-7) have been studied.

2.3. Fermentation process for antibiotic production

It is common for the production of antibiotics to be promoted through easily usable carbon and nitrogen sources (Okada et al., 1997, Jain et al., 2005). Temperatures of 20, 25, 28, 33, and 37 °C, initial pH ranges of 4.0–8.5, fermentation duration ranges of 24 to 120 h were also evaluated. As a result, the antimicrobial activity was assessed (Thi et al., 2019). After incubation, the contents were filtered and the culture filtrates were extracted. The antibacterial activity of the concentrated extracts was determined by agar well diffusion assay (Kumari et al., 2013).

2.4. Medium complexity

Various sources of nitrogen, such as yeast extract, ammonium chloride and peptone, have been tested for maximum antibiotic productivity. (Chatterjee et al., 1981). The media with different concentration of nitrogen source were inoculated with the selected strain (O-7). According to the carbon assimilation test, the selected strain (O-7) uses glucose as a carbon source. In the basal medium, different glucose concentrations were used and antibiotic production was measured.

The pH values of the medium were adjusted and the culture of the strain (O-7) was inoculated and incubated (James et al., 1991), and cultures were studied for the growth and productivity of the antibiotic by cup-plate method (Gesheva et al., 2005).

The optimum temperature for the productivity and growth of the (O-7) strain was determined by keeping the inoculated fermentation media in a shaker incubator (James et al., 1991). Subsequently, the growth of microorganisms and productivity of an antimicrobial activity were determined using cup-plate method (Okada et al., 1997).

Two groups of conical flasks containing media inoculated with the selected strain and incubated in a rotary shaker into two ways for studying light efficacy. Three different sizes of conical flasks (250, 500 and 750 ml) were used and inoculated with the strain (O-7). The incubation of the seeded flasks took place in two ways. The first group incubated in a shaker, and the second group left at room temperature on the bench. The duration of the fermentation process has been optimized to obtain the maximum antibiotic production time for harvesting (James et al., 1991).

2.5. Column chromatography

The sample was fractionated using column chromatography technique, including normal silica gel powder as a stationary phase and different solvents with different polarities as mobile phase. Fractions have been dissolved and used for the antimicrobial study using the standard broth micro dilution method (Duraipandiyan et al., 2009).

2.6. Determination of minimum inhibitory concentration (MIC)

It has been reported earlier that the antimicrobial activity of the compounds from actinomycetes varied depending on the strain from which the compound was obtained, the solvent used for the extraction and the nature of the pathogens tested against such compound (Remya et al., 2008). The minimum inhibitory concentration (MIC) of antimicrobial compounds (Duke, 2016) was determined using the agar dilution method, against six standard organisms: S. aureus, B. subtilis, E. coli, K. pneumoniae, C. albicans, and A. niger.

2.7. Gas Chromatography-Mass spectrometry (GC–MS) analysis

The GC–MS analysis was performed in a Perkin Elmer Clarus 600 gas Chromatograph linked to a mass spectrometer (Turbo mass). The compounds were identified by comparing the spectra with that of the National Institute of Standard and Technology library. The total time needed to analyze a single sample was 61 min.

2.8. Statistical analysis

The statistical methods used in this study include: Descriptive statistics (mean, standard deviation, maximum, minimum, Range, and graphs), T-test for independent samples, and Two Ways (ANOVA) to compare the significant difference between levels. Statistical software (SPSS, version 20) has been used in this study.

3. Results

3.1. Carbon source

Based on the results presented in Table 1, the inhibition zones indicated that glucose was the best sugar among the different types of sugars. It has been observed that 5% concentration of glucose as is optimal for the production of antibiotics for (O-7) strain and 4% for (O-7 exposed), while the concentration of 3% of lactose is optimal for the production of antibiotics for (O-7) strain and 1% for (O-7 exposed) (Table 2).

3.2. Nitrogen source

By determining the influence of nitrogen sources, peptone at a concentration of 1% was found to be a good source of nitrogen for (O-7), and yeast extract for (O-7 exposed) (Table 3).

3.3. pH

From the obtained results, pH 7.0 was found to be the most suitable for both (O-7) and (O-7 exposed) (Table 4).
3.4. Temperature

It was observed that the strain (O-7) and (O-7 exposed) showed a good growth and maximum antibiotic production at 28°C (Table 5).

3.5. Light

The results indicated that the culture flasks incubated in the light produced high activity against the test organisms in both (O-7) and (O-7 exposed) isolates (Figs. 1 and 2).

3.6. Agitation and aeration

No significant effect of aeration and agitation on the productivity of (O-7) and (O-7 exposed) as shown in Table 6.

3.7. Duration of fermentation

Incubation period up to 4 days was found to be significantly optimal for maximum growth as well as maximum antimicrobial agent production (Table 7).

Based upon the above-consolidated results, the fermentation medium and fermentation conditions have been optimized for...
the maximum production of antibiotics and are given as follows: temperature: 28 °C, pH: 7.0, agitation: 180 rpm, fermentation time: 96 h, aeration and light condition.

3.8. Column chromatography

During fermentation, the selected strains produced antibiotics, which were extracted by column chromatography. Two fractions showed good activity against the tested micro-organisms, and then tested for MIC.

3.9. Minimum inhibitory concentration (MIC)

The MIC of the two fractions was found to be 500 μg/ml for the first fraction, and 1000 μg/ml for the second one, against the tested micro-organisms.

3.10. Gas Chromatography-Mass spectrometry (GC–MS)

The GC–MS profiles of the two active fractions and their components are shown in Table 8. For both fractions, the chromatograph showed 23 compounds. Table 8 also showed the components of the previous study for Actinomycete extracts. Nature and biological activities for 14 compounds have been shown (Duke, 2016).

4. Discussion:

Actinomycetes are the largest producers of antimicrobials (Mast and Stegmann, 2019), and this study focused mainly on isolating new types that produce antimicrobials, and tried to extract the largest amount of antimicrobials under different growth conditions, and then their nature was identified using GC–MS.

In this study, the strains of (O-7) were subjected to UV mutagenic treatment. The growth rate of all mutant strains was found to be higher than that of their species. All mutant isolates were found to grow rapidly, covering the entire plate in 4 days. After mutagenic treatment with different time intervals, only one mutant strain was selected and coded as (O-7) exposed. High antimicrobial activity was shown when compared with non-mutated strain. The strain (O-7) exposed enhanced antimicrobial activity against the standard organism (33 mm as a maximum inhibition zone) after exposure to UV radiation for 300 s. With a capacity of 750 ml, the exposed strain (O-7) exhibited maximum production of antibiotics when agitated in flask. Ashock et al. (2014) revealed that their mutated Actinomycetes (UV mutation for 180 s) had shown high antimicrobial activity in comparison

### Table 5

| P-Value | F    | Mean Square | Df | Sum of Squares | Source                | Factors                      | Variables                     |
|---------|------|-------------|----|----------------|-----------------------|------------------------------|-------------------------------|
| 0.01**  | 3.90 | 72.83       | 4  | 291.3          | Between Groups        | O-7 (non-exposed)            | Temperature (in °C)           |
| 0.04*   | 2.57 | 48.23       | 4  | 192.9          | Between Groups        | O-7 (UV) exposed             |                               |
| 0.08    | 2.04 | 42.47       | 8  | 339.7          | Within Groups         | O-7 (non-exposed)            | Diameter of zone of inhibition (mm) |
| 0.00**  | 4.42 | 59.75       | 8  | 478.0          | Between Groups        | O-7 (UV) exposed             |                               |

* P ≤ 0.05 ** P ≤ 0.01.

### Fig. 1.

Effect of light on antimicrobial productivity of non-exposed (O-7) strain.

### Fig. 2.

Effect of light on antimicrobial productivity of exposed (O-7) strain.

### Table 6

| P-Value | df  | T-test | Std. Deviation | Mean group | Factors                      | Variables                     |
|---------|-----|--------|----------------|------------|------------------------------|-------------------------------|
| 0.72    | 13  | 0.37   | 6.54           | 22.56      | Agitation                    | O-7 (un-exposed)              |
| 0.28    | 15  | 1.15   | 4.43           | 20.89      | Static                       |                               |

* P ≤ 0.05 ** P ≤ 0.01.
with non-mutated Actinomycetes by boosting antimicrobial activity against all human bacterial and fungal pathogens examined. Siddique et al. (2014) raised the production of UV mutation Avermectins from mutated Streptomyces avermitilis. Upadhyaya et al. (2014) examined the mutation of Streptomyces for amphotericin B increase and identified that four strains of Streptomyces isolated from the soil of Western Ghats of India generating amphotericin B had been exposed to random UV radiation for improvement of yield. The mutated strains were then tested for antimicrobial B concentrations and antifungal activity using agar well diffusion method, with two mutants showing 13% and 16% higher concentrations than the isolated strains. This mutation could be a very valuable tool to reduce production costs.

During fermentation, sugars such as glucose are commonly used as a carbon source for growth and secondary metabolite production (Silvia et al., 2016). In the current study, the impact of various carbon sources in the production of antibiotics by (O-7) and (O-7) exposed strains was studied. Among the carbon sources, glucose has proven to be a great carbon source for both cell growth and the strain production of antimicrobial metabolites. In this study, the strain was observed to produce elevated amounts of antimicrobial metabolites in the medium supplemented with glucose as the sole carbon source (5% for O-7, 4% for O-7 exposed). Usha et al. (2014) found that glucose is the best source of carbon for producing antibiotics from Streptomyces torulosus KH-4, Staphylococcus aureus and S. kanamyceticus M27. Hemashenpagam (2011) mentioned that Actinomycetes strains generated the highest biomass when glucose was added to the medium. Bashir et al. (2013) noted that the concentration of 3% glucose was optimal for maximum metabolite production. In this research, there were significant differences between the exposure (O-7) and the different glucose concentrations, as well as the diameter of the inhibition zone.

Impact of nitrogen sources on metabolite production was identified by fermentation media with chosen (O-7) strain. The results showed that the optimal source of nitrogen for antibiotic production was peptone for (O-7) and yeast extract for (O-7) exposed strain, respectively. The production of antibiotics by (O-7) exposed in a medium which is supplemented by yeast extract is more than (O-7) produced in the same medium when supplemented by peptone. However, this result was agreed with Jeffrey and Halizah. (2014) who reported that the highest inhibition zone was recorded after peptone was used as a nitrogen source. Rehman et al. (2015) recorded an inhibition zone as wide as 32 mm and 29 mm against E. FBFC-1407 and S. aureus ATCC-259233 in a medium supplemented by sodium nitrate. Although peptone is best for (O-7) strain, and yeast extract for (O-7) exposed. The statistical analysis did not show any significant differences in the use of different nitrogen sources, but there were highly significant differences in the diameter of the inhibition zone.

Highly activity was exhibited at a neutral pH of 7.0. Statistical analysis showed that there were highly significant differences between different pH values with a preference to (O-7) exposed. This finding was agreed with Singh et al. (2014) who reported an optimum pH of 7.0. In a study conducted by Uddin et al. (2013), the optimum pH of the medium was adjusted to the baseline scale of 9.0 for the high activity of Streptomyces albogongus against S. aureus.

Environmental requirements and cultural conditions for the growth and production of (O-7) strain antimicrobial agents have been studied. Temperature of 28 °C was found to be optimal for the highest growth as well as for the maximum production of

**Table 7**

| P-Value | F       | Mean Square | DF | Sum of Squares | Source factors | Variables |
|---------|---------|-------------|----|---------------|----------------|-----------|
| 0.18    | 1.48    | 26.49       | 8  | 211.9         | Between Groups | O-7 (un-exposed) |
|         |         | 17.88       | 57 | 1019.3        | Within Groups  | Time in hours |
| 0.30    | 1.24    | 23.16       | 8  | 185.2         | Between Groups | O-7 (UV) exposed |
|         |         | 18.70       | 56 | 1047.4        | Within Groups  | Diameter of zone of inhibition (nm) |
| 0.00**  | 8.46    | 83.56       | 8  | 668.5         | Between Groups | O-7 (un-exposed) |
|         | 9.87    | 56          | 57 | 562.8         | Within Groups  | O-7 (UV) exposed |
| 0.00**  | 6.14    | 72.01       | 8  | 576.1         | Between Groups | O-7 (UV) exposed |
|         | 11.72   | 56          | 56 | 656.5         | Within Groups  | O-7 (UV) exposed |

*P ≤ 0.05 **P ≤ 0.01.

**Table 8**

| No. | Compound name         | Nature          | Formula | Activity (from literature) |
|-----|-----------------------|-----------------|---------|---------------------------|
| 1   | Hexadecanoic acid     | Fatty acid      | C_{16}H_{32}O_{2} | Antioxidant, hypo cholesterol, emic nematicide, pesticide, lubricant, flavor* |
| 2   | Dodecanoic acid       | Fatty acid      | C_{12}H_{24}O_{2} | Antimicrobial, soaps, shampoo* |
| 3   | 9-Octadecenoic acid   | Fatty acid      | C_{18}H_{34}O_{2} | Anti-inflammatory, cancer preventive, hepato- protective, anti eczemic, anti-acne* |
| 4   | Hexadecane            | Hydrocarbon     | C_{16}H_{34} | Anti-fungal, Anti-bacterial, anti-oxidant activity* |
| 5   | Nonadecane            | Hydrocarbon     | C_{19}H_{36}O | Cyto-toxic effect, anti-microbial * |
| 6   | Heptacosane           | Hydrocarbon     | C_{22}H_{40} | Anti-oxidant activity  |
| 7   | Triacontane           | Hydrocarbon     | C_{24}H_{48} | Cyto-toxic effect, antimicrobial * |
| 8   | 1,2-Benzene di carboxylic acid | Aromatic | C_{8}H_{18}O_{4} | Dyes, perfumes* |
| 9   | Heneicosane           | Hydrocarbon     | C_{28}H_{56} | Antibacterial  |
| 10  | Hexatriacontane       | Hydrocarbon     | C_{30}H_{64} | Antibacterial, antiviral, anticancer  |
| 11  | 2,6,10,15,19,23-Hexamethyl- | Hydrocarbon | C_{32}H_{64} | Antimicrobial  |
| 12  | Cholest-5-en-3-ol     | Sterol          | C_{27}H_{48}O | Drugs for dermatological, skeletal, muscular and neuromuscular disorders  |
| 13  | Hexadecane, 1- (ethoxyloxy) | Hydrocarbon | C_{18}H_{36}O_{2} | Drugs for dermatological disorder, anti-acne agent  |
| 14  | Tritetracontane       | Hydrocarbon     | C_{34}H_{68} | For treating wounds, ulcers, burns, scars and keloids  |

*Duke (2016), *Yogeswari et al (2012), *Kethar et al (2012), *National Library of Medicine, National Center of Biotechnology Information (2020).
antimicrobial agents by strains. In this research, there was a significant difference in the use of different temperatures for (O-7) exposed. The strain (O-7) exposed showed significant differences with the diameter of the zone of inhibition. Singh et al. (2014) noted the same result with the strain S. sananensis SU 118. Rehman et al. (2015) determined that the optimum temperature for Streptomyces sp antibiotic production would be 45 °C and 35 °C.

The use of a wide bottomed flask and agitated deep culture at a speed of 180 rpm increased the production of antibiotics by strain (O-7) exposed to a flask capacity of 750 ml. This result was consistent with Song et al. (2012) who observed that the inhibitory rate reached a peak of about 90% when the speed was 180 rpm. Sharon et al. (2014) revealed that agitation had a direct influence on the growth of Streptomyces sp. KOD10 as agitation impacts the aeration and mixing of nutrients in the fermentation medium.

The crude extracts were obtained at regular intervals (12, 24, 36, 48, 60, 72, 84, 108 and 120 h) from the exposed strain of (O-7) and subjected to secondary screening by agar well-diffusion method. The incubation period up to 4 days was found to be optimal for maximum growth as well as for maximum production of antimicrobial agents. Similarly, Telugu et al. (2014) isolated a strain with good effectiveness after four days of incubation. Singh et al. (2014) observed that seven days were optimal for maximum growth and antimicrobial production, while Bashir et al. (2013) identified that maximum antibacterial activity was noticed after 12 days of incubation.

In the present study, fraction-2 showed MIC values of 500 µg/ml against the following standard pathogens respectively: Aspergillus niger (ATCC 16404), Candida albicans (ATCC 14053), Klebsiella pneumoniae (ATCC 27736), Escherichia coli (ATCC 13706), Shigella sonnei (ATCC 11060), Proteus vulgaris (ATCC 6380), Klebsiella pneumoniae (ATCC 10031) and Escherichia coli (ATCC 10536), and 1000 µg/ml against Enterococcus aerogenes (ATCC 10102) and Klebsiella pneumoniae (ATCC 13882).

From the current research, twenty-three compounds were analyzed by the GC/Ms spectral data developed through the extracts. Depending on the results, the majority of the compounds identified were medicinally important. The major compounds due to the peak area were of Tetracosane, 2,6,10,15,19,23-Hexa-, 1,2- Benzene di carboxylic acid, 2,6,10,15,19,23-Hexa-, 2,6,10,15,19,23-Hexa-, and Dodecanoic acid, 1,2-3- Propane. The four compounds (Hexadecanoic acid, 1, 2-Benzenedi carboxylic acid, Dodecanoic acid and 9-Octadecenoic acid) were reported also by (Jegajeevanram et al., 2014). The findings consistent with Akpuaka et al. (2013), who detected the following six compounds (Hexadecane, Nonadecane, Hexadecanoic acid, 9-Octadecenoic acid, Hexadecosane and Triaccontane) in other type of actinomycetes.

5. Conclusion

The study concluded that the biological compounds produced by the (O-7) strain, isolated from soil, were effective against certain types of bacteria and fungi, and the study also demonstrated that exposure to UV radiation increased the production of these compounds.

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This study was not funded by any company or agency.

Declaration of Competing Interest

The authors declare that they have no competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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