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Dioximino Androstene Derivatives Synthesized Compounds for Anticancer activity using 3- Cell Lines Panel

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Abstract: Steroid derivatives' ability to bind to hormone-related receptors and stop the growth of cancer cells makes them promising anticancer medications. The efficacy of a new class of dioximino androstene derivatives against three distinct cancer cell lines—the brain cancer cell line SF-268, the lung cancer cell line NCI-H460, and the breast cancer cell line MCF-7—was evaluated in this investigation. To determine if these substances were cytotoxic, we used the MTT assay. Cell viability was evaluated after 48 hours of treatment with a consistent dosage. Studies on the structure-activity relationship (SAR) have shown that certain oxime substitutions at C (3) and C (17) significantly increased cytotoxicity. Furthermore, the findings demonstrated significant growth inhibition for certain dioximino androstene derivatives. Molecular docking studies revealed that these drugs have strong interactions with significant cancer-related protein targets. Furthermore, dioximino androstene derivatives offer therapeutic potential and are excellent candidates for the development of anticancer drugs, according to the ADME/Tox data. To optimise these compounds for medicine, further thorough study is strongly recommended, including in vivo evaluations.

Keywords: Dioximino Androstene, Anticancer Activity, MTT Assay, Cytotoxicity, Structure-Activity Relationship, Drug Development

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INTRODUCTION

Novel Therapeutics for Cancer and Its Metastatic Spread

Cancer remains one of the most challenging diseases to treat due to the staggering number of new cases discovered each year. The unregulated development, invasion, and metastasis of cancer cells has made the search for effective therapies for the disease a significant global concern. Surgery, radiation, and chemotherapy are examples of conventional cancer therapies that may not always target cancer cells precisely and may have major side effects. However, these are examples of the more conventional methods of treating cancer. New, less harmful anticancer therapies are urgently needed, and steroid derivatives have been extensively studied as potential alternatives. Because of their structural resemblance to natural hormones, androstene-based compounds have garnered a lot of attention among these molecules. This is because they could participate in important biological functions that are connected to the development of cancer.

Steroidal Compounds and Their Function in Cancer Treatment

The therapeutic potential of steroidal drugs has been the subject of extensive investigation for quite some time, with a focus on hormone-dependent malignancies including prostate and breast cancer. It is feasible

to enhance the compound's anticancer powers by making changes to the steroidal backbone, which greatly increases biological activity. Because of their ability to interact with hormone receptors, modify cellular signalling pathways, and trigger apoptosis in cancer cells, the dioximino androstene derivatives are very intriguing. These derivatives vary structurally from androstene due to the inclusion of oxime (-C=NOH) groups to certain locations within their structures. A more effective cytotoxic effect on different types of cancer cells is the rationale for this modification.

Derivatives of Dioximino Androstene: Chemical Importance and Action Mechanism

It has been observed that the incorporation of oxime functional groups into the structure of androstene compounds has a significant influence on the biological activity of these compounds. The lipophilicity of oxime derivatives is enhanced, which enables them to engage with intracellular targets and achieve increased membrane permeability. To add insult to injury, these modifications have the potential to increase the binding affinity for essential receptors and enzymes that play a role in the genesis and spread of tumours. Oxime-containing steroids have been shown to have the potential to induce cell death by reducing reactive oxygen species (ROS) levels, activating caspases, and depolarising mitochondrial membranes, according to some study. Because of the features that they possess, dioximino androstene derivatives are an intriguing chemical family that might be used in future research on cancer treatments.

Cancer Cell Line-Based In Vitro Evaluation of Dioximino Androstene Derivatives

The anticancer potential of freshly manufactured compounds can only be determined by reliable in vitro screening methods. The MTT assay, which tracks the metabolic activity of living cells, is a commonly used way to determine cytotoxicity. In this study, the anticancer properties of dioximino androstene derivatives were evaluated using a panel of three cell lines: MCF-7 (breast cancer), NCI-H460 (lung cancer), and SF-268 (central nervous system cancer). These cell lines may stand in for different types of cancer due to their distinct biological features. The MTT test provides quantitative data on cell viability, which may be used to measure the synthesised compounds' cytotoxic potential and structure-activity relationships (SAR).

Investigations into Molecular Docking and Structure-Activity Relationships (SAR)

Having a grasp of the connection between the chemical structure and the biological activity of a medication is necessary for taking a reasonable approach to the process of drug production. The structure-activity relationship (SAR) of dioximino androstene derivatives was analysed in order to assess the anticancer activity of these compounds. In order to determine the parameters that influence cytotoxicity, we investigated a variety of aspects, including electrical properties, steric effects, and the physical position of oxime substitutions. Additionally, molecular docking studies were used by the researchers in order to investigate the manner in which these chemicals attached to cancer-related targets such as oestrogen and androgen receptors, in addition to kinases that are involved in the process of cell proliferation. Through the use of these computer approaches, we gained a great deal of knowledge on the potential action mechanisms of the synthesised pharmaceuticals.

In the process of drug development, the importance of ADME/Tox Analysis

A chemical must possess favourable pharmacokinetic and toxicological properties in order for it to be

considered a prospective candidate for future drug development. This is because these features are essential for the creation of a drug. Investigations known as absorption, distribution, metabolism, and excretion (ADME) are used in order to develop forecasts about the manner in which a chemical would behave inside the human body. On the other hand, the toxicity assessments, also known as Tox evaluations, are used to assess the potential adverse effects that the chemical may have. All of the most promising dioximino androstene derivatives were subjected to in silico ADME/Tox predictions as part of this inquiry. The purpose of this investigation was to determine the possible medicinal applications of these compounds. Parameters such as lipophilicity (LogP), solubility, plasma protein binding, and expected toxicity were analysed in order to guarantee that these medications had suitable pharmacokinetic profiles for future study. This was done in order to ensure that these drugs would be adequately used.

OBJECTIVES

1. Research on Dioximino Androstene Derivatives: Their Chemical Importance and Action Mechanism.
2. Investigating Steroidal Compounds' Function in Cancer Treatment

EXPERIMENTAL

The majority of the aldehydes and aluminium isopropoxide were provided by Fluka Chemie, which is located in Buchs, Switzerland. The following chemicals were provided by Qualigen Fine chemicals, which is located in Mumbai, India: iodine, sodium sulphate, acetone, methanol, chloroform, toluene, and cyclohexanone. E. Merck, based in Mumbai, India, was the company that provided the silica gel G source. Without charging any fees, the dehydroepiandrosterone acetate was provided by Cipla Ltd., which is based in Mumbai, India. Melting points that have not been adjusted are presented. Tetramethyl silane (TMS) was used as the internal standard for the 1H-NMR spectra that were obtained from the Varian EM-390 (90 MHz), AC-300F (300 MHz), and EM-360 (60 MHz) nuclear magnetic resonance (NMR) instruments. Infrared spectra were obtained by means of a spectrophotometer equipped with a Perkin-Elmer 882, whilst UV spectra were obtained via the use of a Lamda 15. In a setting that included ethanol, the ultraviolet spectra were collected. For the purpose of acquiring infrared spectra, potassium bromide pellets were used. The purity of the compounds was validated by the use of elemental analysis and thin-layer chromatography. The results obtained from the elemental analyses carried out on a Perkin-Elmer-2400 indicated that the values for carbon, hydrogen, and nitrogen were within a range of ±0.4% of the theoretical values. The V6-11-250J70 S and the CEC-21-110B Finnigan Mat 1210 or Micro Mass 7070 were both equipped with a direct intake system that was used to record mass spectra at a voltage of 70 eV. Anhydrous sodium sulphate was used as the drying agent, while iodine vapours were used as the developing agent. At a temperature of 1100 degrees Celsius for a period of thirty minutes, iodine vapours were used in order to visualise the TLC plates that had been made in accordance with Stahl's (E. Merck) instructions. The solvent that was employed was EtOAc. The use of anhydrous sodium sulphate was employed as a method of drying. When it came time to employ any of the solvents, they were all dehydrated and redistilled in line with the methods that had been developed.

An Aldol Condensation-Based General Procedure for 16-Substituted Benzylidene Derivative Synthesis 6–13

Twenty millilitres of methanol were modified by the addition of the following components: one gramme of dehydroepiandrosterone with a concentration of 3.47 millimoles, one gramme of sodium hydroxide, and one gramme of aldehyde in the appropriate quantity. While the mixture was at room temperature, it was continuously stirred for a period of one hour. On the basis of the TLC, we were able to determine when the reaction had finished. In order to complete the reaction, cold water was added to the mixture. The precipitate that was produced as a result of this process was filtered, washed with water, dried, and then crystallised from myethanol in order to get the 16-substituted benzylidene derivatives of androsten-5-en-3-ol.

16-(2-Pyridylmethylene)-17-oxo-5-androsten-3-ol 6

Six (1.0 g) was obtained by condensing DHA with 2-pyridinecarboxaldehyde (Picon aldehyde, 1.7 ml, 14.02 mmol).

16-(3-Pyridylmethylene)-17-oxo-5-androsten-3-ol 7

3-pyridinecarboxaldehyde (nicotinaldehyde, 1.5 ml, 14.02 mmol) was used to condense DHA, resulting in 7 (0.8 g).

16-[4-(2-Dimethylaminoethoxy)-3-methoxybenzyli-dene]-17-oxo-5-androsten-3-ol 8

4-(2-dimethylaminoethoxy)-3-methoxy benzaldehyde (1.5 ml, 7.51 mmol) was condensed with DHA to produce 8 (1.2 g).

16-[3-Methoxy-4-(2-morpholin-4-yl-ethoxy) benzyli- dene]-17-oxo-5-androsten-3-ol 9

3-methoxy-4-(2-morpholin-4-yl-ethoxy) benzaldehyde (1.5 g, 5.66 mmol) was condensed with DHA to produce 9 (1.20 g).

16-(4-Methoxybenzylidene)-17-oxo-5-androsten-3- ol 10

DHA was condensed with 4-methoxybenzaldehyde (0.75 g, 11.03 mmol), to yield 10 (0.4 g).

General Preparation of 16-Substituted Benzylidene 3,17-Diones 14-21

It was possible for the oppenauer oxidation to take place since the aldol product (6-13, 1.0 g) was dissolved in a combination of cyclohexanone (10 ml) and dry toluene (150 ml). Through the process of azeotropic distillation, any and all traces of moisture that were present in the combination were thoroughly eliminated. During the subsequent stages of the distillation process, which were carried out at a leisurely rate, a solution that was composed of 1.0 grammes of aluminium isopropoxide in 30 millilitres of dry toluene was progressively added. After being exposed to a period of reflux that lasted for four hours, the reaction mixture was permitted to rest at room temperature for a duration of twelve hours. Following the completion of the filtering procedure, the residue that was left behind was washed with dry toluene. After the organic solvents had been completely extracted from the combined filtrate and washings, they were put through steam distillation until they were completely removed from the mixture. The 14–21 were made by

letting the solid residue to settle for a length of time, sifting it, washing it with water, drying it, and then crystallising it from acetone. This process was repeated many times.

Pharmacology

The National Cancer Institute (NCI) in Bethesda, USA, tested the medicines' biological activity in three cell lines in vitro. For cancer screening, human tumour cell lines were grown in RPMI 1640 media with 2 mM L-glutamine and 5% foetal bovine serum. Screening was done in 96-well microtiter plates with 5,000–40,000 cells/well. The cell densities in each well were determined from their doubling times. A 100-microlitre inoculation was used. After cell inoculation, microtiter plates were incubated for 24 hours at 37°C, 5% CO2, 95% air, and 100% humidity. This prepared the plates for experimental drug loading.

Experimental drugs were soluble in dimethyl sulfoxide and evaluated at 400 times the recommended quantity. The plates were incubated at 37 degrees Celsius with 5% CO2, 95% air, and 100% relative humidity for 48 hours after the medicine was administered. Cold TCA on adhering cells ended the experiment. Adding 50 µl of cold TCA at 50% (w/v) resulted in a final concentration of 10% TCA. Cells were incubated at 4°C for 60 minutes. After draining the supernatant, the plates were washed five times with tap water and dried naturally. Plaques were incubated at room temperature for 10 minutes after adding 100 µl of 0.4% (w/v) Sulforhodamine B (SRB) solution in 1% acetic acid to each well. The plates were air-dried after staining to eliminate unbound colour.

Five 1% acetic acid washes followed. After dissolving the bound dye with a 10 mM trizma base, an automatic plate reader measured absorbance at 515 nm. We utilised the same procedures to finish the experiment using suspension cells, except for adding 50 µl of 80% TCA (final concentration, 16 percent TCA) to the wells to fix the settling cells. Seven absorbance measurements are utilised to compute growth percentages at each of the five medication concentration levels. Time zero (Tz), control growth (C), and drug-induced growth at each of the five concentration levels are measured. Growth inhibition percentage was determined.

RESULTS AND DISCUSSION

Chemistry

DHA 5 was condensed by pyridine. Pyridine, Picon aldehyde, three-carbox-aldehyde (nicotineldehyde), and four-dimethyl aminoethoxy are involved. This category includes methoxy benzaldehyde, 3-methoxybenzaldehyde, -4-[ethoxy compound of 2-morpholino]benzaldehyde, p-nitro benzaldehyde, p-isopropyl, 3,4-dimethoxybenzaldehyde, and others. aldol condensation in basic medium produces aldol compounds 6–13 in that order. Oppenauer oxidation of cyclohexanone and aluminium isopropoxide in toluene at refluxing temperature generated compounds 14–21. According to the conventional approach, hydroxylamine hydrochloride and sodium acetate trihydrate were oximated in aldehyde to create free alcohol dioximino derivatives 22–29 (Scheme 1).

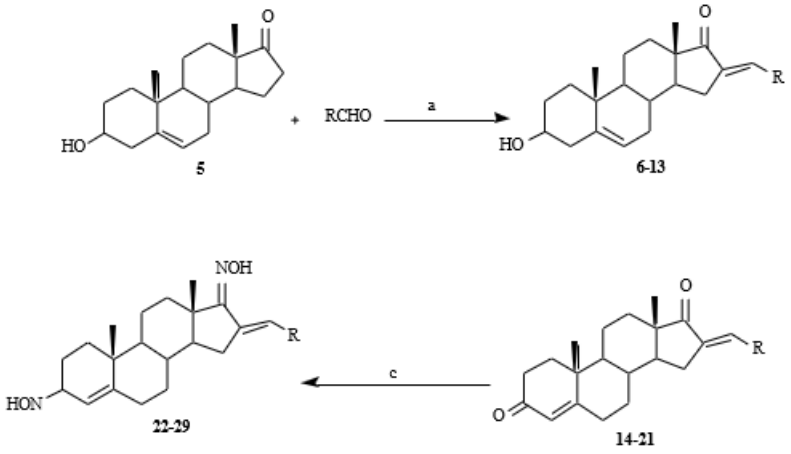
In addition to elemental analysis, UV, IR, 1H-NMR, mass spectroscopy, and elemental analysis were used in order to validate the structures of all of the compounds 6-29. At around 3400 and 1715 cm-1, respectively, the infrared spectra of compounds 6-13 revealed the presence of an O-H stretch and a C=O

stretch. The oxidation of hydroxyl functionality at position 3 in the steroid molecule was verified by the presence of C=O stretch at around 1680 and 1715 cm-1 for carbonyl functionalities at position 3 and 17 respectively in compounds 14-21. Additionally, the lack of O-H stretching in the infrared spectrum provided further evidence of this oxidation. In the infrared spectra, the compounds 22-29 exhibited the lack of a C=O stretch and the presence of a >N=O-H stretch at 3300 cm-1. The nuclear magnetic resonance (NMR) spectra of the proton displayed a peak for >N=OH at ± 7.5-10 ppm, which vanished with the exchange of D2O. Table I contains all you need to know about the physical constants of each and every chemical.

Biological Activity

For the purpose of determining the potential activity of 22–28 of the eight dioximino androstene derivatives that were synthesised, the National Cancer Institute in Bethesda, which is located in the United States of America, used computerised molecular modelling and a selection procedure implemented inside their databases. A panel of three cell lines was used to evaluate the anticancer activity of the selected medicines. These cell lines were MCF-7 (breast), NCI-H460 (lung), and SF-268 (control nervous system).

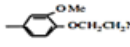
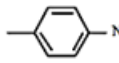
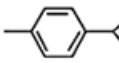
After allowing the compounds to incubate for a period of forty-eight hours, they were tested in vitro against these three cell lines using a single concentration of one thousand equal to four millimolar. During the process of measuring the activity, the percentage of cell growth inhibition was used. The results of this test indicate that compounds 22–28 (Table II) are also active. All of the compounds that have shown statistically significant antineoplastic activity will be subjected to a complete anticancer test using sixty different cell lines respectively.



Scheme 1. The synthesis process for compounds 6-29 is outlined below.

Sodium hydroxide must be shaken at normal temperature, cyclohexanone and aluminium isopropoxide must be refluxed, and hydroxylamine hydrochloride and sodium acetate trihydrate must be shaken.

Table I. Compounds 6-29's Physical Constants

Compd	R	Yield (%)	mp (^{0}C)	Mol. Formula	MW	UVλ_{max} (MeOH) (nm)	IR,[1] H-NMR, MS
6 (DPJ-957)		72.9	205-210	$C_{25}H_{31}NO_2$	377.51	295.6 (logε 4.30) and 270.8 (logε 4.12)	IR : 3200, 2980, 1718, 1630, 1580 and 1460 cm^{-1}.[1]H-NMR ($CDCl_3$) : δ 1.08 (s, 3H, 18-C*H*$_3$), 1.11 (s, 3*H*, 19-C*H*$_3$), 3.52 (m, 1H, 3α-*H*), 5.40 (d, 1H, 6-C*H*), 7.21 (m, 1H, 5-C*H* aromatic proton), 7.40 (m, 1H, 3-C*H* aromatic proton), 7.44 (s) and 7.47 (s) [0.9:1 area ratio, integrating for 1H, vinyl-*H* of 16-(2-pyridylmethylene)], 7.72 (m, 1H, 4-C*H* aromatic proton) and 8.70 (s, 1H, 6-C*H* aromatic proton) ppm.
7 (DPJ-916)		58.36	260-264	$C_{25}H_{31}NO_2$	377.51	281.6 (logε 4.32)	IR : 3350, 2920, 1715, 1630 and 900 cm $^{-1}$.[1]H-NMR ($CDCl_3$) : δ 0.99 (s, 3H, 18-C*H*$_3$), 1.08 (s, 3H, 19-C*H*$_3$), 3.54 (t, 1H, 3α-*H*), 5.4 (d, 1H, 6-C*H*), 7.35-7.40 [m, 2H, one vinyl-*H* of 16-(3-pyridylmethylene) and 5-C*H* aromatic proton], 7.83 (d, 1H, J_o= 7.8, 4-C*H* aromatic proton), 8.57 (d, 1H, 6-C*H* aromatic proton) and 8.80 (s, 1H, 2-C*H* aromatic proton) ppm.
8 (DPJ-1012)		54.52	190-194	$C_{31}H_{43}NO_4$	493.66	265.0 (logε 4.33)	IR :3240, 2970, 1705, 1610, 1595, 1250 and 800 cm^{-1}.[1]H-NMR ($CDCl_3$) :δ 0.98 (s, 3H, 18-C*H*$_3$), 1.07 (s, 3H, 19-C*H*$_3$), 2.43 [s, 6H, -N-(C*H*$_3$)$_2$], 2.9 (t, 2H, -C*H*$_2$-N<), 3.88 (s, 3H, -OC*H*$_3$), 4.19 (t, 2H, -OC*H*$_2$-), 5.39 (d, 1H, 6-C*H*), 6.93 (d, 1H, J_o=8.2, 5-C*H* aromatic proton), 7.05 (d, 1H, J_m=1.4, 2-C*H*, aromatic proton), 7.14 (dd, J_m=1.3,J_o=8.3, 6-C*H* aromatic proton) and 7.38 {s, 1H, vinyl-*H* of 16-[4-(2-dimethylamino)-3-methoxybenzylidene]} ppm.
10 (DPJ-863)		61.64	220	$C_{27}H_{34}O_3$	406.54	321.4 (logε 4.40)	IR : 3500, 2935, 1705, 1620, 1595 and 1260 cm^{-1}.[1]H-NMR ($CDCl_3$) : δ 0.97 (s, 3H, 18-C*H*$_3$), 1.08 (s, 3H, 19-C*H*$_3$), 3.52 (m, 1H, 3α-*H*), 3.85 (s, 3H, -OC*H*$_3$), 5.40 (d, 1H, 6-C*H*), 6.94 (d, 2H, J_o=8.7 Hz, 3-C*H* and 5-C*H* aromatic protons), 7.40 (s, 1H, vinyl-*H* of 16-(4-methoxybenzylidene)] and 7.51 (d, 2H, J_o=8.7 Hz, 2-C*H* and 6-C*H* aromatic protons) ppm. MS : m/z 407 [M$^+$]
11 (DPJ-814)		55	270-272	$C_{28}H_{36}O_4$	436.57	333.4 (logε 4.40)and 244.0 (logε 4.04)	IR : 3510, 2900, 1720, 1610,1510, 1240 and 1110 cm^{-1}.[1]H-NMR ($CDCl_3$) : δ 0.98 (s, 3H, 18-C*H*$_3$), 1.07 (s, 3H, 19-C*H*$_3$), 3.52 (m, 1H, 3α-*H*), 3.91 (s, 3H, -OC*H*$_3$), 3.92 (s, 3H, -OC*H*$_3$) 5.40 (d, 1H, 6-C*H*), 6.92 (d, 1H, J_o=8.5 Hz, 5-C*H* aromatic proton), 7.06 (d, 1H, J_m=1.6 Hz, 2-C*H* aromatic proton), 7.17 (dd, 1H, J_m=1.6 Hz, J_o=6.6 Hz, J_m=1.8 Hz, 6-C*H* aromatic proton) and 7.39 (s, 1H, vinyl-*H* of 16-(3,4dimethoxybenzylidene] ppm. MS: m/z 437 [M$^+$]
12 (DPJ-849)		45.73	240-242	$C_{26}H_{31}NO_4$	421.52	314.6 (logε 4.49)	IR$_{vmax}$ (KBr) : 3400, 2920, 1720, 1620, 900 and 852 cm^{-1}.[1]H-NMR ($CDCl_3$) : δ 1.00 (s, 3H, 18-C*H*$_3$), 1.08 (s, 3H, 19-C*H*$_3$), 3.54 (m, 1H, 3α-*H*) 5.40 (d, 1H, 6-C*H*), 7.45 [s, 1H,vinyl-*H* of 16-(4-nitrobenzylidene)], 7.67 (d, 2H, J_o=8.7 Hz, 2-C*H* and 6-C*H* aromatic protons) and 8.27 (d, 2H, J_o=8.7 Hz, 3-C*H* and 5-C*H* aromatic protons)ppm. MS:m/z 421[M$^+$]
13 (DPJ-986)		65.79	120-125	$C_{29}H_{38}O_2$	418.59	305.8 (logε 4.22)	IR : 3380, 2980, 1710, 1610, 1040 and 900 cm^{-1}.[1]H-NMR ($CDCl_3$) : δ 0.98 (s, 3H, 18-C*H*$_3$), 1.07 (s, 3H, 19-C*H*$_3$), 1.26 [d, 6H, CH-(C*H*$_3$)$_2$], 2.91 [m, 1H, C*H*-(CH$_3$)$_2$], 3.54 (m, 1H, 3α-*H*), 5.40 (d, 1H, 6-C*H*), 7.28 (d, 2H, J_o=8.0 Hz, 3-C*H* and 5-C*H* aromatic protons), 7.43 [s, 1H, vinyl-*H* of 16-(4-isopropylbenzylidene)] and 7.48 (d, 2H, J_o=9.9 Hz, 2-C*H* and 6-C*H* aromatic proton) ppm.
14 (DPJ-995)		90.48	188-190	$C_{25}H_{29}NO_2$	375.49	296.0 (logε 4.18) and 243.8 (logε 4.18)	IR : 2980, 1720, 1670, 1590, 1430 and 900 cm $^{-1}$.[1]H-NMR ($CDCl_3$) : δ 1.01 (s, 3H, 18-C*H*$_3$), 1.25 (s, 3H, 19-C*H*$_3$), 5.76 (d, 1H, 4-C*H*), 7.21 (m, 1H, 5-C*H* aromatic proton), 7.39 (m, 1H, 3-C*H* aromatic proton), 7.43 (s) and 7.45 (s) [0.7:1 area ratio, integrating for 1H, vinyl *H* of 16-(2-pyridyl methylene)], 7.71 (m, 1H, 4-C*H* aromatic proton) and 8.71 (d, 1H, 6-C*H* aromatic proton) ppm. MS: m/z 375 [M$^+$]
15 (DPJ-917)		59.68	202-208	$C_{25}H_{29}NO_2$	375.49	281.0 (logε 4.34) and 242.0 (logε 4.30)	IR : 2980, 1715, 1670 and 900 cm $^{-1}$.[1]H-NMR ($CDCl_3$) : δ 1.03 (s, 3H, 18-C*H*$_3$), 1.26 (s, 3H, 19-C*H*$_3$), 5.77 (s, 1H, 4-C*H*), 7.35-7.41 [m, 2H, one vinyl-*H* of 16-(3-pyridylmethylene) and 5-C*H* aromatic proton], 7.82 (d, 1H, J_o= 7.9, 4-C*H* aromatic proton), 8.58 (m, 1H, 6-C*H* aromatic proton) and 8.79 (d, 1H, J_p=1.0, 2-C*H* aromatic proton)ppm. MS: m/z 375 [M$^+$].

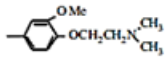
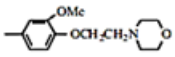
16 (DPJ-1013)		99	78-82	$C_{31}H_{41}NO_4$	491.64	334.0 (log ε 4.25) and 241.4 (log ε 4.31)	IR:2980,1705,1680,1620,1510,1260 and 800 cm^{-1}. ^{1}H-NMR ($CDCl_3$) : δ 1.0 (s, 3H, 18-CH_3), 1.25 (s, 3H, 19-CH_3), 2.36 [s, 6H,N-(CH_3) $_2$], 2.80 (t, 2H, -CH_2-N<), 3.89 (s, 3H, -OCH_3), 4.16 (t, 2H, -OCH_2-), 5.76 (s, 1H, 4-CH), 6.93 (d, 1H, J_o=8.3, 5-CH aromatic proton), 7.05 (d, 1H, J_m=1.2, 2-CH aromatic proton), 7.14 (dd, 1H, J_m=1.3, 1.6 and J_o=6.8, 6-CH aromatic proton) and 7.40 {s,1H,vinyl-H of 16-(4-(2-dimethylaminoethoxy)-3-methoxy benzylidene)} ppm.
17 (DPJ-1066)		85.34	62-66	$C_{33}H_{43}NO_5$	533.63	334.4 (log ε 4.36) and 241.0 (log ε 4.44)	IR : 2920, 1705, 1665, 1440, 1245 and 900 cm^{-1}.^{1}H-NMR ($CDCl_3$) : δ1.01 (s, 3H, 18-CH_3), 1.25 (s, 3H, 19-CH_3), 2.67 (br, 4H, N-methylenes of morpholino function), 2.92 (t, 2H, CH_2-N<), 3.79 (m, 4H, O-methylenes of morpholino function), 3.89 (s, 3H, -OCH_3-), 4.24 (t, 2H, -OCH_2-), 5.77 (s, 1H, 4-CH), 6.93 (d, 1H, J_o=8.5 Hz, 5-CH aromatic proton), 7.06 (s, 1H, 2-CH aromatic proton), 7.16 (d, 1H, J_o=8.3 Hz, 6-CH aromatic proton) and 7.40 {s, 1H, vinyl-H of 16-[3-methoxy-4-(2-morpholino-4-yl-ethoxy) benzylidene]} ppm.

Table 2. Results of an in vitro cancer test with three cell lines, sample concentration 10-4 mL

Compound No.	Prefix NSC	Growth Percentages			
		(Lung) NCI-H460	(Breast) MCF7	(CNS) SF-268	Activity
22	S724180	82	98	96	Inactive
23	S718810	-43	11	17	Active
24	S722348	0	0	-1	Active
25	S723370	-	-	-	Active
26	S716660	-10	7	-1	Active
27	S716264	11	4	8	Active
28	S718243	5	15	34	Active

CONCLUSION

Based on the findings of this research, it can be concluded that the oximino functionality plays a key part in determining the anticancer activity of steroidal derivatives that have been substituted with 16-benzylidene molecules. Through the introduction of a 3-pyridylmethylene group into the 16-benzylidene substituted dioximino series, the highest level of activity was achieved in comparison to the other series that were synthesised. The alteration of aromatic benzaldehydes that are connected to position 16 of the steroid nucleus is another method that may be used to acquire the tumoricidal capabilities of the dioximino

molecule by modifying it. These modifications may include the addition of substituents like methoxy and/or nitro, among other possible modifications. The findings of this sort of study shed light on the significance of adding 3,17-dioximino activities into the development of steroidal anticancer medications in the years to come.

References

1. Remers, W.A. In 'Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry'; 9th edition, pp.345, Delgado, J.N.; Remers, W.A. Ed.; J.B. Lippincott Co., 1991.
2. Brodie, A.M.H.; Coombes, R.C.; Dowsett, M. J. Steroid Biochem.1987, 27, 899-903.
3. Budzar, A. U. Clin. Breast Cancer 2003, (Suppl. 2), S84-S88.
4. O'Reilly, J.M.; Brueggemeier, R. W. J. Steroid Biochem. Mol. Biol. 1996, 59(1), 93-102.
5. Rodríguez, J.; Nunez, L.; Peixinho, S.; Jimenez, C. Tetrahedron Lett. 1997, 38, 1833.
6. Deive, N.; Rodríguez, J.; Jimenez, C. J. Med. Chem. 2001, 44,2612-2618.
7. Christiansen, R.G.; Clinton, R.O.; Dean, J. W. U.S. Pat. 316364,1964, [Chem. Abstr. 1965, 62, 7834].
8. Easthem, J.F.; Taranishi, R. 'In Organic Synthesis', Vol.2, pp.1- 28, Adams, R., Ed.; John Wiley and Sons, Inc: New York, 1960.
9. Hershberg, E. B. J. Org. Chem. , 1948, 13, 542-546.
10. Vogel, C.L. Anticancer Drugs 2003, 14 (4), 265-273.
11. Bohl, M. In Theoratical Investigation on Steroid Structure and Quantitative Structure Activity Relationships, Bohl, M.; Duax, W.L., Ed.; CRC Press: Boca Raton, FL, 1992, pp. 185-186.
12. Waller, C.L.; Juma, B.W.; Gray, L.E.; Kelce, W.R.; Toxicol. Appl. Pharmacol., 1996, 137, 219.
13. Chattopadhaya, R,; Jindal, D.P.; Minu, M; Gupta, R. Arzneimittel Forschung., 2004, 54, 551.
14. Christiansen, R.G.; Clinton, R.O.; Dean, J. W.; U.S.Pat. 316364, 1964, [Chem. Abstr.1965, 62, 7834].