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Synthesis, Characterization and Anticancer Evaluation of 1-(5-Substituted-1H-Indol-3-Yl)-3-(P-Substituted-Benzyl) Prop-2-En-1-One Derivatives

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KEYWORDS

Indole Derivative, Anti-cancer screening, Human Colorectal Cell, Irinotecan, *In-vitro* Cell line.

ABSTRACT:

Objectives: To synthesize and characterized new 1-(5-substituted-1H-indol-3-yl)-3-(p-substituted-benzyl) prop-2-en-1-one derivatives and screen their *in-vitro* anticancer activity.

Methods: By reacting 2-amino-5-substituted-benzaldehyde with derivatives of 1-chloropropan-2-one,1-(5-substituted-1H-indol-3-yl)-3-(p-substituted-benzyl)prop-2-en-1-one indole chalcone compounds were synthesized. Based on FT-IR, H^1 and C^{13} NMR, MS spectrum investigations, the newly synthesized compounds were described. Using the MTT assay, all the synthesized compounds were tested for their ability to inhibit the growth of human colorectal cells (HCT-116).

Results: According to FT-IR, H^1 and C^{13} NMR spectrum data, the indole substituted chalcone compounds (SBS1-7) were successfully synthesized by condensation method. A dose-dependent suppression of cell growth was produced by all synthesized substances. The IC_{50} values for all synthesized compounds were obtained from range 10.70 to 553.94 µM. Among the synthesized chalcone compounds SBS3 and SBS4 were showed to be the most potent anticancer activity.

Conclusions: These findings suggested that chalcone derivatives having indole ring may serve as promising new targets for the development of anticancer drugs.

1. Introduction

Cancer has emerged as one of the most difficult conditions for people to treat among all the illnesses that affect them, and as of now, there are no practical and widely applicable treatments. Colon cancer is caused by genetic mutations and their functional effects, which cause the normal colonic epithelium to transform into malignant tumors, including polyposis and nonpolyposis, including dysplasia and metaplasia [1]. According to research, the average age of invasive cancer diagnosis in developed nations is around 70 years old [2]. Person age [3], a history of chronic disorders such inflammatory bowel disease [4], crohn's disease [5], and a sedentary lifestyle, as well as obesity [6], poor nutritional habits [7], smoking, and alcohol use [8] are all linked to an increased risk of developing colon related cancer (CRC). Therefore, a continuously aging population, poor modern eating habits, and an increase in risk factors like smoking, low physical activity, and obesity are all contributing to an increase in the incidence of CRC in developed countries [9].

One of the primary objectives of medicinal chemistry is to create of new anticancer therapeutics. Major issues

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with cancer treatment include cytotoxicity and genotoxicity of anticancer medications to normal cells, which raises the possibility of causing subsequent malignancy. A dose of an anticancer medicine required to kill tumor cells is frequently toxic to normal tissue and causes several side effects, which in turn reduces the effectiveness of the treatment. Therefore, one of the most urgent health issues is the need for new, effective, selective, and less toxic anticancer medicines [10]. The creation and discovery of innovative, selective anticancer medicines free of many of the unfavorable side effects of traditional anticancer treatments have been the focus of intense research in recent years. It will take some time to complete the synthesis of a newer class of anticancer drugs [11].

The structural characteristics of nitrogen-containing heterocyclic, also known as N-heterocyclic, have become widely used in medicinal chemistry. Indole motifs have drawn a lot of attention among the many N-heterocyclic since they can be found in medicines, proteins, amino acids, and other bioactive substances [12]. The indole and its derivatives are a significant class of heterocyclic compounds with a variety of biological effects. The literatures reveal that compounds containing indole possess biological properties such as anticonvulsant [13], antiproliferative and proapoptotic [14], anti-inflammatory and antipyretic activities [15], activity against *vaccinia* virus and *cowpox* virus [16], analgesic and antiulcer [17], antimicrobial [18], anti-infective [19], antibacterial, antifungal, and anti-HIV [20].

The present work synthesizes and characterizes a new series of indole chalcone derivatives and their anticancer efficacy against cancer cell lines has been assessed using the MTT technique.

2. Materials and Methods

2.1 Materials

Analytical reagent grade materials were used for all of the solvents, reagents, and catalysts. The following items were purchased from Himedia (Mumbai, India): Dimethyl sulfoxide (DMSO), Fetal bovine serum (FBS), l-glutamine, Dulbecco's modified eagle's medium (DMEM), Trypsin EDTA, Penicillin, Amphotericin B, and Streptomycin. Trypan blue and 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were bought from Sigma Aldrich. The supplier of Irinotecan (CAS no. 9768244-5) was Biopharma LLP in India. The methods described in the literature were used to create all derivatives.

2.2 General Characterization Techniques

The uncorrected melting points (MP) were calculated using electrical melting point apparatus and expressed in degrees Celsius (°C). On a Bruker FT-IR spectrometer, the compounds' IR spectra were captured using KBr disc. The Bruker apparatus was used to scan the H^1 and C^{13} NMR. Chemical shifts are measured using DMSO as the solvent and are represented in d (ppm) in relation to TMS as the internal standard. The mass spectra were captured on an Agilent 7890Å gas chromatography operational with mass spectroscopy. By employing silica gel glass plates as the stationary phase, benzene and ethanol (9:1) as the mobile phase, and thin layer chromatography to determine the purity of the chemicals. Iodine vapor or UV light (254 nm) were used to see the spots.

2.3 Chemistry

2.3.1 Synthesis of 1-(5-subsituted-1H-indol-3-yl)-3-(p-subsituted-benzyl)prop-2-en-1-one

The general synthesis scheme of 1-(5-subsituted-1H-indol-3-yl)-3-(p-subsituted-benzyl)prop-2-en-1-one was shown in Figure 1. The 5 grams K_2CO_3 and 5 grams 2-amino-5-substituted-benzaldehyde **(a)** combination was agitated at room temperature in 50 ml dry acetone for an hour. The reaction was started by adding 4 ml of 1-chloropropan-2-one **(b)** dropwise to the reaction mixture at 0-5 °C. The mixture was then agitated at room temperature for 30 minutes before refluxed. Thin-layer chromatography (TLC) was performed to check the completion of reaction. After the mixture was placed into crushed ice, the solid precipitate that was created, one-(5-substituted-1H-indol-3-yl)ethan-1-one (c). This precipitated was further filtered and re-crystallized in ethanol. One of the commercially available aromatic aldehydes, 4-substituted benzaldehyde **(d),** was combined with 1-(5-substituted-1H-indol-3-yl)ethan-1-one **(c)** (0.6 gm), in methanol and the mixture was agitated in an ice bath for 15 minutes. Then, 3.5 ml of aqueous sodium hydroxide (NaOH) was gradually added to this solution, and it was agitated for 5 hours at room temperature. The substance

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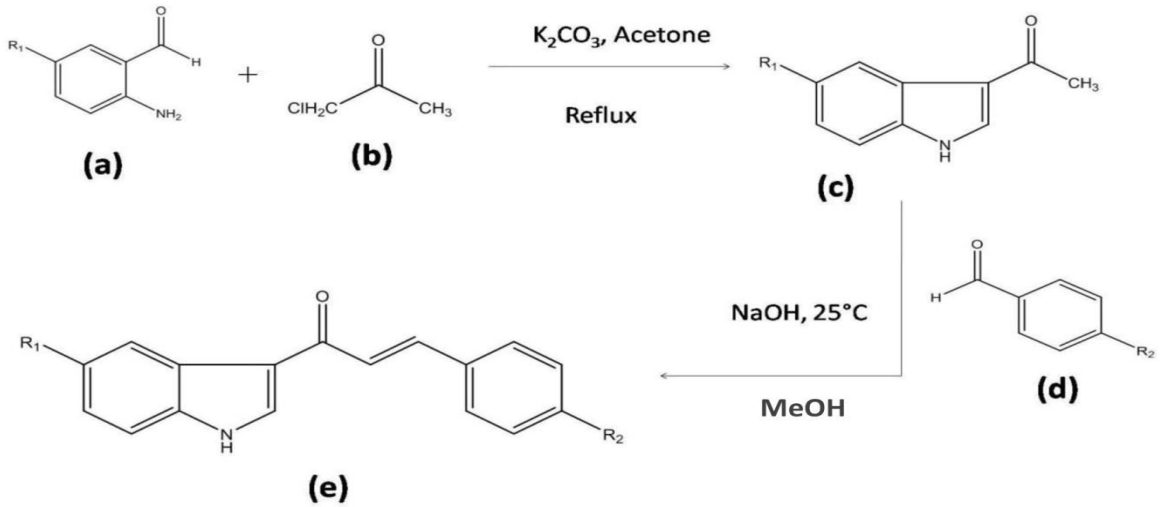
for the reaction was poured into the frigid water. The precipitated solid 1-(5-substituted-1H-indol-3-yl)-3-(p-substituted-benzyl)prop-2-en-1-one **(e)** was collected on a paper filter and crystallized from ethanol to get the target compounds (SBS1-7) after the pH was adjusted up to 7 using hydrochloric acid (HCl) solution.

2.3.2 Spectral data of synthesized compounds (SBS1-7)

2.3.2.2 Spectral data of (E)-4-(3-(1H-indol-3-yl)acryloyl)benzene sulfonic acid (SBS2). MP (231-234°C), % Yield (72%), IR υ (cm-^{1}): 3407 (N-H), 3111 (C-H Alkene), 2528 (S-H), 1728 (C=O), 1669 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 1H, OH), 11.96 (s, 1H, NH), 7.03-7.78 (m, 4H, Ar-H), 7.68-8.04 (m, 4H, Ar-H), 2.57 (s, 3H, methyl), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 21.7, 111.0, 113.9, 120.1, 120.8, 126.2, 127.3, 128.9, 129.9, 130.8, 134.1, 137.9, 145.1, 189.7. ESI: m/z value 327.06.



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SBS1:	$R_1 = H$	$R_2 = C_6H_4SO_3H$	**SBS5:**	$R_1 = C_6H_4SO_3H$	$R_2 = CH_3$
SBS2:	$R_1 = H$	$R_2 = SO_3H$	**SBS6:**	$R_1 = CH_3$	$R_2 = CH_3$
SBS3:	$R_1 = CH_3$	$R_2 = C_6H_4SO_2H$	**SBS7:**	$R_2 = C_6H_4SO_3H$	$R_2 = C_6H_4SO_3H$
SBS4:	$R_1 = CH_3$	$R_2 = SO_3H$			

Figure 1: General synthesis of 1-(5-substituted-1H-indol-3-yl)-3-(p-substituted-benzyl)prop-2-en-1-one **(e)**

2.3.2.1 Spectral data of (E)-4'-(3-(1H-indol-3-yl)acryloyl)-[1,1'-biphenyl]-4-sulfonic acid (SBS1).

MP (222-224°C), % Yield (61%), IR υ (cm-1): 3406 (N-H), 3060 (C-H Alkene), 2540 (S-H), 1725 (C=O), 1626 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 1H, OH), 11.96 (s, 1H, NH), 7.03-7.78 (m, 4H, Ar-H), 7.68-8.04 (m, 8H, Ar-H), 2.56 (s, 3H, methyl), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 21.7, 111.0, 113.9, 120.1, 120.8, 126.2, 126.8, 127.3, 128.6, 129.8, 130.4, 130.8, 134.4, 136.8, 145.1, 146.6, 189.7. ESI: m/z value 403.09.

2.3.2.3 Spectral data of (E)-4'-(3-(5-methyl-1H-indol-3-yl)acryloyl)-[1,1'-biphenyl]-4-sulfonic acid (SBS3). MP (198-203°C), % Yield (63%), IR υ (cm-^{1}): 3408 (N-H), 3058 (C-H Alkene), 2539 (S-H), 1723 (C=O), 1623 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 1H, OH), 11.96 (s, 1H, NH), 7.03-7.78 (m, 4H, Ar-H), 7.68-8.04 (m, 8H, Ar-H), 2.56 (s, 3H, methyl), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 21.3, 111.6, 113.9, 116.8, 119.2, 126.8, 127.3, 127.8, 128.9, 129.8, 130.4, 130.8, 136.8, 143.7, 145.1, 146.6, 189.7. ESI: m/z value 418.11.

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2.3.2.4 Spectral data of (E)-4-(3-(5-methyl-1H-indol-3-yl)acryloyl)benzene sulfonic acid (SBS4). MP (202-204°C), % Yield (67%), IR υ (cm-^{1}): 3407 (N-H), 3037 (C-H Alkene), 2468 (S-H), 1747 (C=O), 1630 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 1H, OH), 11.96 (s, 1H, NH), 7.27-7.78 (m, 4H, Ar-H), 7.15-8.04 (m, 10H, Ar-H), 2.34 (s, 3H, methyl), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 47.7, 116.6, 113.9, 119.2, 126.8, 127.3,127.8, 128.9, 129.8, 130.4, 130.8, 136.0, 143.7, 145.1, 145.8, 189.7. ESI: m/z value 341.07.

2.3.2.5 Spectral data of (E)-4-(3-(3-oxo-3-(p-tolyl)prop-1-en-1-yl)-1H-indol-5-yl)benzene sulfonic acid (SBS5). MP (161-163°C), % Yield (70%), IR υ (cm-^{1}): 3408 (N-H), 3058 (C-H Alkene), 2539 (S-H), 1723 (C=O), 1623 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 1H, OH), 11.96 (s, 1H, NH), 7.03-7.78 (m, 4H, Ar-H), 7.68-8.04 (m, 8H, Ar-H), 2.56 (s, 3H, methyl), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 47.7, 115.5, 111.6, 113.9, 116.8, 118.6, 119.2, 126.8, 127.3, 127.7, 128.9, 130.4, 130.8, 136.0, 143.7, 145.1, 189.7. ESI: m/z value 417.10.

2.3.2.6 Spectral data of (E)-3-(5-methyl-1H-indol-3-yl)-1-(p-tolyl)prop-2-en-1-oneacid (SBS6). MP (173-175°C), % Yield (68%), IR υ (cm-^{1}): 3400 (N-H), 3085 (C-H Alkene), 2541, 1741 (C=O), 1623 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 2H, OH), 11.96 (s, 1H, NH), 7.27-7.78 (m, 5H, Ar-H), 7.68-8.04 (m, 4H, Ar-H), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 111.5, 111.6, 113.9, 116.8, 119.2, 126.8, 127.3, 127.8, 128.4, 128.6, 128.9, 129.8, 130.8, 136.0, 139.9, 143.7, 145.1, 145.8, 189.7. ESI: m/z value 275.35.

2.3.2.7 Spectral data of (E)-4'-(3-(5-(4-sulfophenyl)-1H-indol-3-yl)acryloyl)-[1,1'-biphenyl]-4-sulfonic acid (SBS7). MP (152-155°C), % Yield (57%), IR υ (cm-^{1}): 3400 (N-H), 3085 (C-H Alkene), 2541 (S-H), 1741 (C=O), 1623 (C=C). H^{1} NMR (DMSO) d ppm: 4.2 (s, 2H, OH), 11.96 (s, 1H, NH), 7.27-7.78 (m, 5H, Ar-H), 7.68-8.04 (m, 4H, Ar-H), 7.60-8.06 (m, 2H, ethylene). C^{13} NMR (DMSO) 47.7, 111.5, 111.6, 113.9, 116.8, 118.6, 119.2, 126.8, 127.3, 127.8, 128.4, 128.6, 128.9, 129.8, 130.4, 130.8, 132.7, 136.0, 136.8, 140.8, 143.7, 145.1, 146.6, 189.7. ESI: m/z value 527.09.

2.4 In Vitro Anticancer Activity

2.4.1 Cell lines and cell culture

In our investigation, human colorectal cell lines (HCT-116) were utilized. Human colorectal cell lines (HCT-116) were provided by NCCS (the National Centre for Cell Science, Pune, India). In 75 cm^{2} culture flasks, HCT-116 cell lines were grown in DMEM media supplemented with 1% L-Glutamine, 10% Fetal Bovine Serum, streptomycin (1 g/L), penicillin (1 U/mL), and amphotericin B (0.25 g) antibiotics. All cells were maintained at 37°C throughout the tests using a humidified carbon dioxide incubator (5% CO_2 + 95% O_2; Panasonic, Japan). Trypan blue at 0.4% was used to determine the cell viability ratios prior to the application of chalcone chemicals. We did not start the studies if the viability ratios were less than 90%. [21]

2.4.2 Sample preparation

In DMSO, stock solutions (100 M) of synthetic indole molecules were made. To create working concentrations (1, 5, 25, 50, and 100 M), the stock solution of indole compounds was serially diluted with DMSO and DMEM. In the experiment, DMSO served as the positive control while Irinotecan served as the standard medication. The recommended vehicle controls were made with a maximum DMSO content of 0.004%.

2.4.3 Cell viability analysis (MTT Assay)

The synthesized indole derivatives were examined utilizing the MTT assay technique for their anticancer activity against HCT-116 cell lines. Active mitochondria changed the pale yellow tetrazolium salt, MTT, into a dark blue formazan, which was identified by UV spectroscopy (Shimadzu 1800) [22]. Confluent cells were sown in 96-well plates with 5×10^{3} cells in each well after being taken from the flasks using trypsin-EDTA solution. At 37°C, the plates were incubated for 24 hours. The cancer cells were then treated with DMSO (for the positive control group) and various doses of indole compounds (SBS1-7) in DMSO (1, 5, 25, 50, and 100 M), and the cells were then incubated for 24 hours at 37°C in a humidified incubator with 5% CO_2 and 95% O_2. After incubating the plates for 24 hours with indole compounds, MTT solution added to each well. The absorbance was then measured using a UV Spectrophotometer (Shimadzu

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1800) at a wavelength of 570 nm. The tests were repeated thrice.

The following formula was used to compute the proportion of viable cells:

$$Cell\ Viability = \frac{\text{Test absorbance} - \text{Blank absorbance}}{\text{Vehicle control absorbance} - \text{Blank absorbance}} \text{ X } 100$$

To get the IC_{50} values, the percentages of cell viability were plotted against the logarithmic concentrations of indole produced compounds using a non-linear regression curve.

2.5 Statistical Analysis

All quantitative data were given as mean ± standard deviation (SD). The one-way analysis of variance (ANOVA) followed by Tukey's multiple comparisons test was used to identify statistical significant differences for continuous variables. The IC_{50} and log IC_{50} values were determined by using % cell viability values of compounds by nonlinear curve fit (Dose Response) method. All analysis was done by OriginPro statistical software. All *p*-values ≤ 0.05 were considered as statistical significant.

3. Result and discussion

3.1 Chemistry

The new 1-(5-substituted-1H-indole-2-yl) ethan-1-one was obtained from aldol condensation reaction of 2 amino-5-substituted Benzaldehyde and 1-chloropropan-2-one. A series of indole substituted chalcones (SBS1-7) were synthesized by condensation of 1-(5-substituted-1H-indole-2-yl) ethan-1-one and various commercially available aromatic aldehydes. For the synthesis of chalcones, the most common route is the base catalyzed Claisen-Schmidt reaction involving condensation of a benzaldehyde derivative with an acetophenone derivative in methanol with sodium hydroxide catalyst [23-25]. Physical data for all synthesized chalcones derivatives are shown in Table 1.

The indole substituted chalcones derivatives (SBS1-7) were characterized by elemental analysis, FT-IR, H^1 and C^{13} NMR spectroscopy techniques. Anticancer activity against HCT-116 was investigated in these newly synthesized (SBS1-7).

In the FT-IR spectra of 1-(5-substituted-1H-indol-3-yl)-3-(p-substituted-benzyl)prop-2-en-1-one, C=O stretching vibration was observed at 1723 cm−1. The synthetic chalcones SBS1-7 showed characteristic bands between 1723 and 1747 cm−1 (C=O stretching at chalcone) and between 1623 and 1669 cm−1 (C=C stretching at chalcone).

The most characteristic signals in H^1 NMR spectra of the indole substituted chalcones were observed at 11.96 ppm (s, 1H, NH at indole ring) and at 7.60–8.06 ppm (α- H and β-H of chalcone moiety). The carbonyl carbon was observed at about 189.7 ppm in the C^{13} NMR spectra of SBS1-7.

3.2. Anticancer Activity.

The synthesized substituted chalcone compounds (SBS1-7) were tested in-vitro anticancer activity against the HCT-116 cancer cell lines at five different concentrations (1, 5, 25, 50, and 100 µM) by using the MTT assay. The cell viability percentage of synthesized compounds was determined.

Table 1: Physical data of all synthesized test compounds (SBS1-7)

S. No.	Compound	Molecular Formula	R1	R2	Molecular Weight	% Yield	Melting Point (°C)
1	SBS1	$C_{23}H_{17}NO_4S$	H	$C_6H_4SO_3H$	403.45	61	222-224
2	SBS2	$C_{17}H_{13}NO_4S$	H	SO_3H	327.35	72	231-234
3	SBS3	$C_{24}H_{19}NO_4S$	CH_3	$C_6H_4SO_3H$	417.48	63	198-203
4	SBS4	$C_{18}H_{15}NO_4S$	CH_3	SO_3H	341.38	67	202-204
5	SBS5	$C_{24}H_{19}NO_4S$	$C_6H_4SO_3H$	CH_3	417.48	70	161-163
6	SBS6	$C_{19}H_{17}NO$	CH_3	CH_3	275.35	68	173-175
7	SBS7	$C_{29}H_{21}NO_7S_2$	$C_6H_4SO_3H$	$C_6H_4SO_3H$	559.61	57	152-155

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The effects of the synthesized chalcone compounds (SBS1-7) on cell viability as determined 24 hours after exposure are shown in Figure 2. The log IC_{50} values of the synthesized chalcone compounds (SBS1-7) were determined by using inhibition percentage values by OriginPro statistical software. The log IC_{50} values of the synthesized chalcone compounds were shown in Table 2.

On HCT-116 cell lines, the synthesized chalcone compounds (SBS1-7) exhibit anticancer activity ($p < 0.05$). All synthesized substances resulted in a dose-dependent suppression of cell proliferation. All the compounds at 100 µM concentrations significantly reduced the viability percentage of HCT-116 cells ($p < 0.001$).

Table 2: *In-vitro* cell viability results for synthesized compounds

Compound	HCT-116 Cell Line			
	IC_{50} (µM)	Standard Error	Log IC_{50} (µM)	Standard Error
SBS1	135.42	17.86	2.13	0.05
SBS2	247.45	88.11	2.39	0.15
SBS3	10.7	0.94	1.02	0.03
SBS4	13.83	1.19	1.14	0.03
SBS5	553.94	698.61	2.74	0.54
SBS6	59.84	3.25	1.77	0.02
SBS7	482.71	437.20	2.68	0.39
STD (Irinotecan)	12.21	1.07	1.08	0.03

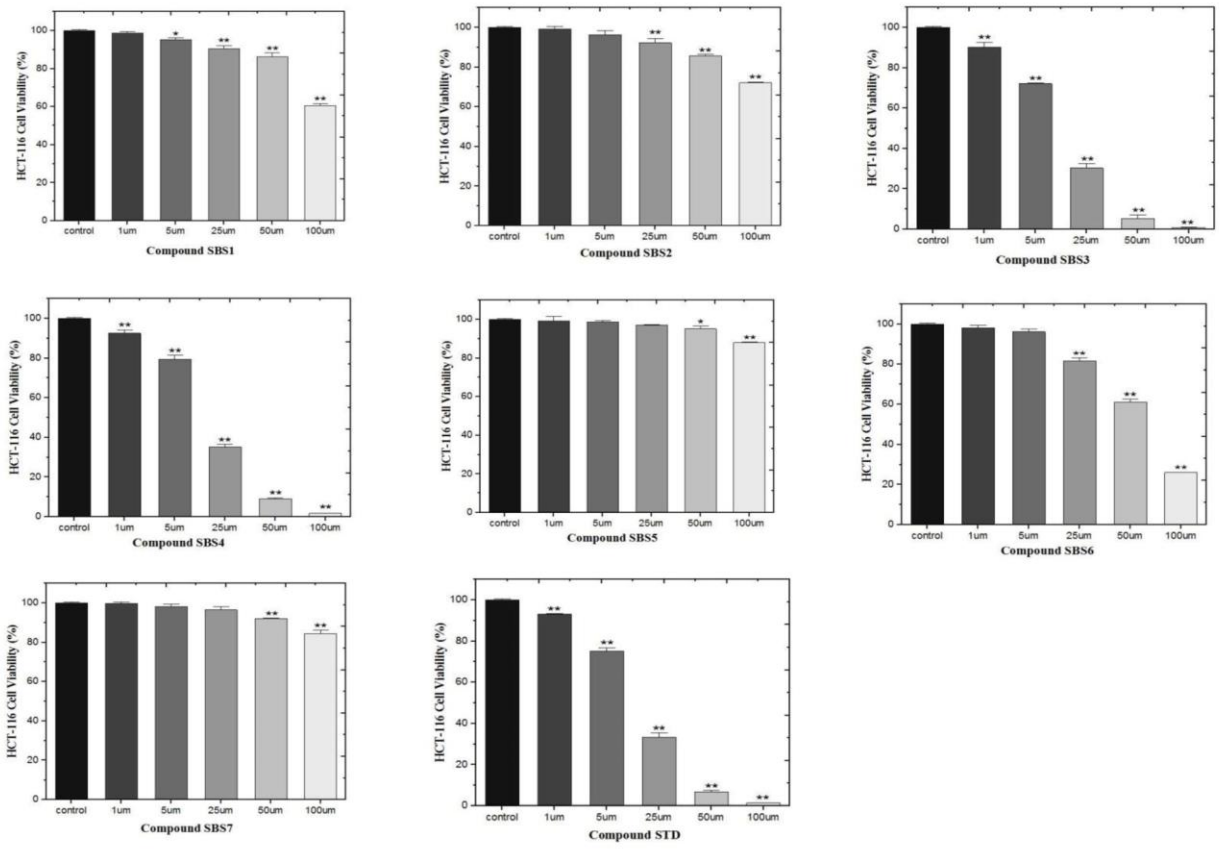

Figure 2: The Cell viability (%) of HCT-116 cells following the exposure of various concentrations of the compounds [SBS1-7] and untreated control cell for 24 h [* $p < 0.05$. ** $p < 0.001$]

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Compounds SBS3 and SBS4 were found to be the most potent against HCT-116 cell lines among the synthesized chalcone compounds. According to structure activity relationships indole substituted chalcone compounds showed more potent activities than the unsubstituted indole chalcone compounds. Overall indole chalcone compounds show anticancer activity. These findings implied the potential use of indole modified chalcone as lead molecules in the synthesis of new, highly effective anticancer drugs.

4. Conclusion

The *in-vitro* anticancer activity of synthesized 1-(5-Substituted-1H-Indol-3-yl)-3-(p-substituted-benzyl)prop-2-en-1-one chalcone compounds was assessed using the MTT assay. The indole substituted chalcone compounds exhibit high anticancer activity against HCT-116 cell lines ($p < 0.001$). These findings suggested that chalcone derivatives having indole ring would be beneficial in the future for development of new anticancer drug.

5. Acknowledgement

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6. Conflict of interest

All authors have approved the final manuscript, and the authors declare that they have no conflicts of interest to disclose.

Refrences

1. Ilyas M., Straub J., Tomlinson I.P.M., Bodmer W.F.,1999. Genetic pathways in colorectal and other cancers. European Journal of Cancer. 35, 1986–2002.
2. Siegel R., DeSantis C., Virgo K., Stein K., Mariotto A., Smith T., Cooper D., Gansler T., Lerro C., Fedewa S., 2012. Cancer treatment and survivorship statistics, A Cancer J. Clin. 62, 220–241.
3. Levin B., Lieberman D.A., Farland M.B., Andrews K.S., Brooks D., Bond J., Dash C., Giardiello F.M., Glick S., Johnson D., 2008. Screening and Surveillance for the Early Detection of Colorectal Cancer and Adenomatous Polyps, A Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. CA Cancer J. Clin. 58,130–160.
4. Eaden J.A., Abrams K.R., Mayberry J.F., 2001. The risk of colorectal cancer in ulcerative colitis, A meta-analysis Gut. 48,526–535.
5. Canavan C., Abrams K., Mayberry J., 2006. Meta-analysis: Colorectal and small bowel cancer risk in patients with Crohn's disease. Aliment. Pharmacol. Ther. 23,1097–1104.
6. Martinez-Useros J., Garcia-Foncillas J., 2016. Obesity and colorectal cancer: Molecular features of adipose tissue. J. Transl. Med. 14,1–12.
7. Willett W.C., 2005. Diet and Cancer: An Evolving Picture. JAMA. 293,233–234.
8. Pöschl G., Seitz H.K., 2004. Alcohol and Cancer. Alcohol. 39,155–165.
9. Kuipers E.J., Grady W.M., Lieberman D., Seufferlein T., Sung J.J., Boelens P.G., Velde D.C.J.H., Watanabe T., 2015. Colorectal cancer. Nat. Rev. Dis. Primers. 1,15065-15067.
10. Aboraia A.R., Abdel-Rahman H.M., Mahfouz N.M., EL-Gendy M.A., 2006. Novel 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione derivatives: Promising anticancer agents. Bioorganic & Medicinal Chemistry. 14, 1236–1246.
11. Gudipati R., Anreddy R.N.R., Manda S., 2011. Synthesis, characterization and anticancer activity of certain 3-{4-(5-mercapto-1,3,4-oxadiazole-2-yl)phenylimino}indolin-2-one derivatives. Saudi Pharmaceutical Journal. 19,153–158.
12. Shaikh T.M.A., Debebe H., 2020. Synthesis and Evaluation of Antimicrobial Activities of Novel N-Substituted Indole Derivatives. Journal of Chemistry. 3,1-9.
13. Verma M., 2004. Anticonvulsant activity of Schiff bases of isatin derivatives, Acta Pharm. 54,49–56.
14. Cane A., Tournaire M.C., Barritault D., Arias M.C., 2000. The endogenous oxindoles 5-hydroxyoxindole and isatin are antiproliferative and proapoptotic. Biochemical and Biophysical Research Communications. 276,379–384.
15. Sridhar S.K., Ramesh A., 2001. Synthesis and pharmacological activities of hydrazones, schiff and mannich bases of isatin derivatives. Biol. Pharm. Bull. 24(10), 1149—1152.

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16. Quenelle D.C., Keith K.A., Kern E.R., 2006. In vitro and in vivo evaluation of isatin-thiosemicarbazone and marboran against vaccinia and cowpox virus infections. Antiviral Research. 71, 24–30.
17. Bhandari S.V., Bothara K.G., Raut M.K., Patil A.A., Sarkate A.P., Mokale V.J., 2008. Design, synthesis and evaluation of antiinflammatory, analgesic and ulcerogenicity studies of novel s-substituted phenacyl-1,3,4-oxadiazole-2-thiol and schiff bases of diclofenac acid as nonulcerogenic derivatives. *Bioorg*. Med. Chem. 16, 1822–1831.
18. Khanum S.A., Shashikanth S., Umesha S., Kavitha R., 2005. Synthesis and antimicrobial study of novel heterocyclic compounds from hydroxybenzophenones. European Journal of Medicinal Chemistry. 40, 1156–1162.
19. Kucukguzel S.G., Kucukguzel I., Tatar E., Rollas S., Sahin F., Gulluce M., Clercq E.D., Kabasakal L., 2007. Synthesis of some novel heterocyclic compounds derived from diflunisal hydrazide as potential anti-infective and anti-inflammatory agents. European Journal of Medicinal Chemistry. 42, 893-901.
20. Pandeya S.N., Sriram D., Nath G., Clercq E.D., 1999. Synthesis, antibacterial, antifungal and anti-HIV evaluation of Schiff and Mannich bases of isatin derivatives with 3-amino-2-methylmercapto quinazolin-4(3*H)* -one. Pharmaceutica Acta Helvetiae. 74, 11–17.
21. Kucukbay H., Mumcu A., Tekin S., Sandal S., 2016. Synthesis and evaluation of novel N,N'-disubstituted benzimidazolium bromides salts as antitumor agents, Turkish Journal of Chemistry. 40, 393–401.
22. Kolocouris N, Foscolos GB, Kolocouris A et al., 1994. Synthesis and antiviral activity evaluation of some aminoadamantane derivatives, Journal of Medicinal Chemistry. 18: 2896–2902.
23. Souza G.B., Santos T.A.C., Silva A.P.S., Barreiros A.L.B.S., Nardelli V.B., Siqueira I.B., Dolabella S.S., Costa E.V., Alves P.B., Scher R., Fernandes R.P.M., 2022. Synthesis of chalcone derivatives by Claisen-Schmidt condensation and *in vitro* analyses of their antiprotozoal activities. Nat Prod Res. 4, 1-8.
24. Dong F., Jian C., Zhenghao F., Kai G., Zuliang L., 2008 Synthesis of chalcones via Claisen–Schmidt condensation reaction catalyzed by acyclic acidic ionic liquids. Catalysis Communications. 9, 1924–1927.
25. Dave S.S., Ghatolea A.M., Rahatgaonkar A.M., Chorghade M.S., Chauhan P.M.S., Srivastava K.,2009. Experimental and computational evaluation of new quinolinyl chalcones as potent antiplasmodialagents. Indian Journal of Chemistry. 48(B), 1780-1793.