Synthesis, spectroscopic, dielectric, molecular docking and DFT studies of (3E)-3-(4-methylbenzylidene)-3,4-dihydro-2H-chromen-2-one: an anticancer agent

T. Beena¹, L. Sudha¹, A. Nataraj¹, V. Balachandran², D. Kannan³ and M. N. Ponnuswamy⁴*

Abstract

Background: Coumarin (2H-chromen-2-one) and its derivatives have a wide range of biological and pharmaceutical activities. They possess antitumor, anti-HIV, anticoagulant, antimicrobial, antioxidant, and anti-inflammatory activities. Synthesis and isolation of coumarins from different species have attracted the attention of medicinal chemists. Herein, we report the synthesis, molecular structure, dielectric, anticancer activity and docking studies with the potential target protein tankyrase.

Results: Molecular structure of (3E)-3-(4-methylbenzylidene)-3,4-dihydro-2H-chromen-2-one (MBDC) is derived from quantum chemical calculations and compared with the experimental results. Intramolecular interactions, stabilization energies, and charge delocalization are calculated by NBO analysis. NLO property and dielectric quantities have also been determined. It indicates the formation of a hydrogen bonding between –OH group of alcohol and C=O of coumarin. The relaxation time increases with the increase of bond length confirming the degree of cooperation and depends upon the shape and size of the molecules. The molecule under study has shown good anticancer activity against MCF-7 and HT-29 cell lines. Molecular docking studies indicate that the MBDC binds with protein.

Conclusions: In this study, the compound (3E)-3-(4-methylbenzylidene)-3,4-dihydro-2H-chromen-2-one was synthesized and characterized by spectroscopic studies. The computed and experimental results of NMR study are tabulated. The dielectric relaxation studies show the existence of molecular interactions between MBDC and alcohol. Theoretical results of MBDC molecules provide the way to predict various binding sites through molecular modeling and these results also support that the chromen substitution is more active in the entire molecule. Molecular docking study shows that MBDC binds well in the active site of tankyrase and interact with the amino acid residues. These results are compared with the anti-cancer drug molecule warfarin derivative. The results suggest that both molecules have comparable interactions and better docking scores. The results of the antiproliferative activity of MBDC and Warfarin derivative against MCF-7 breast cancer and HT-29 colon cancer cell lines at different concentrations exhibited significant cytotoxicity. The estimated half maximal inhibitory concentration (IC 50) value for MBDC and Warfarin derivative was 15.6 and 31.2 μg/ml, respectively. This enhanced cytotoxicity of MBDC in MCF-7 breast cancer and HT-29 colon cancer cell lines may be due to their efficient targeted binding and eventual uptake by the cells. Hence the compound MBDC may be considered as a drug molecule for cancer.

Keywords: Chromen, DFT, Dielectric studies, Molecular docking, Anti-cancer activity

*Correspondence: mnpsy2004@yahoo.com

© The Author(s) 2017. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.
Background

Coumarin (2H-chromen-2-one) is one of the important secondary metabolic derivatives which occurs naturally in several plant families. Coumarins are used as a fragrance in food and cosmetic products. Coumarins are widely distributed in the plant kingdom and are present in notable amounts in several species, such as Umbelliferae, Rutaceae and Compositae.

Coumarin and its derivatives have a wide range of biological and pharmaceutical activities. They possess antitumor [1], anti-HIV [2], anticoagulant [3], antimicrobial [4], antioxidant [5] and anti-inflammatory [6] activities. The antitumor activities of coumarin compounds have been extensively examined [7]. Synthesis and isolation of coumarins and its derivatives from different species have attracted the attention of medicinal chemists. The spectroscopic studies led to the beneficial effects on human health and their vibrational characteristics [8, 9].

Herein, we report the synthesis, the computed electronic structure and their properties in comparison with experimental FT-IR, FT Raman, UV and NMR spectra. Further, intra and inter molecular interactions, HOMO–LUMO energies, dipole moment and NLO property have been determined. The dielectric studies confirm the molecular interactions and the strength of hydrogen bonding between the molecule and the solvent ethanol. In addition, anti-cancer activity against MCF-7 and HT-29 cell lines and molecular docking studies have also been performed.

Experimental

Preparation of MBDC

MBDC was synthesised from the mixture of methyl 2-[hydroxy(4-methylphenyl)methyl]prop-2-enoate (0.206 g, 1 mmol) and phenol (0.094 g, 1 mmol) in CH2Cl2 solvent and allowed to cool at 0 °C. To this solution, concentrated H2SO4 (0.098 g, 1 mmol) was added and stirred well at room temperature (Scheme 1). After completion of the reaction as indicated by TLC, the reaction mixture was neutralized with 1 M NaHCO3 and then extracted with CH2Cl2. The combined organic layers were washed with brine (2 × 10 ml) and dried over anhydrous sodium sulfate. The organic layer was evaporated and the residue was purified by column chromatography on silica gel (100–200) mesh, using ethyl acetate and hexane (1:9) as solvents. The pure form of the title compound was obtained as a colorless solid (0.162 g). Yield: 65%, melting point: 132–134 °C.

Instrumentation

FTIR, FT-Raman, UV–Vis and NMR spectra were recorded using Bruker IFS 66 V spectrometer, FRA 106 Raman module equipped with Nd:YAG laser source, Beckman DU640 UV/Vis spectrophotometer and Bruker Bio Spin NMR spectrometer with CDCl3 as solvent, respectively. The dielectric constant (ε′) and dielectric loss (ε″) at microwave frequency were determined by X-Band microwave bench and the dielectric constant (ε∞) at optical frequency was determined by Abbe’s refractometer equipped by M/s. Vidyut Yantra, India. The static dielectric constant (ε0) was measured by LCR meter supplied by M/s. Wissenschaifltich Technische, Werkstatter, Germany. Anticancer activity for two cell lines was obtained from National Centre for Cell Sciences, Pune (NCCS).

Cell line and culture

MCF-7 and HT-29 cell lines were obtained from National Centre for Cell Sciences, Pune (NCCS). The cells were maintained in Minimal Essential Medium supplemented with 10% FBS, penicillin (100 U/ml), and streptomycin (100 μg/ml) in a humidified atmosphere of 5% CO2 at 37 °C.

Reagents

MEM was purchased from Hi Media Laboratories, Fetal Bovine Serum (FBS) was purchased from Cistron laboratories trypsin, methylthiazolyl diphenyl-tetrazolium bromide (MTT) and dimethyl sulfoxide (DMSO) were purchased from (Sisco Research Laboratory Chemicals, Mumbai). All of other chemicals and reagents were obtained from Sigma Aldrich, Mumbai.

In vitro assay for anticancer activity (MTT assay)

Cells (1 × 10^5/well) were plated in 24-well plates and incubated at 37 °C with 5% CO2 condition. After the cell reaches the confluence, the various concentrations of the samples were added and incubated for 24 h. After incubation, the sample was removed from the well and washed.
with phosphate-buffered saline (pH 7.4) or MEM without serum. 100 µl/well (5 mg/ml) of 0.5% 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-tetrazolium bromide (MTT) was added and incubated for 4 h. After incubation, 1 ml of DMSO was added in all the wells. The absorbance at 570 nm was measured with UV-Spectrophotometer using DMSO as the blank. The %cell viability was calculated using the following formula:

\[
\text{%cell viability} = \left( \frac{A_{570} \text{ of treated cells}}{A_{570} \text{ of control cells}} \right) \times 100
\]

**Computational methods**

Electronic structure and optimized geometrical parameters were calculated by density functional theory (DFT) using Gaussian 09W software package [10] with B3LYP/6-31 + G(d,p) basis set method and Gauss-View molecular visualization program package on a personal computer [11]. Vibrational normal mode wavenumbers of MBDC were derived with IR intensity and Raman intensity. The entire vibrational assignments were executed on the basis of the potential energy distribution (PED) of vibrational modes from VEDA 4 program and calculated with scaled quantum mechanical (SQM) method. The X-ray crystal structure of tankyrase (PDB ID: 4L2K) [12] was obtained from Protein Data Bank (PDB). All docking calculations were performed using induced-fit-docking module of Schrödinger suite [13].

**Results and discussion**

**Molecular geometry**

The optimized molecular structure of MBDC along with the numbering of atoms is shown in Fig. 1. The calculated and experimental bond lengths and bond angles are presented in Table 1. The molecular structure of the compound is obtained from Gaussian 09W and GAUSSVIEW program. The optimized structural parameters (bond lengths and bond angles) calculated by DFT/B3LYP with 6-31 + G(d,p) basis set are compared with experimentally available X-ray data for benzylidene [14] and coumarin [15].

From the structural data, it is observed that the various C–C bond distances calculated between the rings 1 and 2 and C–H bond lengths are comparable with that of the experimental values of benzylidene and coumarins. The influence of substituent groups on C–C bond distances of ring carbon atoms seems to be negligibly small except that of C3–C4 (1.404 Å) bond length which is slightly longer than the normal value.

The calculated bond lengths of C8–C13 and C4–C20, are 1.491 and 1.509 Å in the present molecule and comparable with the experimental values of 1.491 and 1.499 Å. The experimental value for the bond C13–O7 (1.261 Å) is little longer than the calculated value 1.211 Å. The C–H bond length variations are due to the different substituent’s in the ring and other atoms [16]. The hyperconjugative interaction effect leads to the deviation of bond angle for C10–C11–O12 (121.79°) from the standard value (120.8°).

**Vibrational spectra**

The title compound possesses C₃ point group symmetry and the available 93 normal modes of vibrations are distributed into two types, namely A’ (in-plane) and A” (out-plane). The irreducible representation for the C₃
Carbon–hydrogen vibrations
The C–H stretching vibrations are expected to appear at 3100–2900 cm\(^{-1}\) [17] with multiple weak bands. The four hydrogen atoms left around each benzene ring give rise to a couple of C–H stretching, C–H in-plane bending and C–H out-of-plane bending vibrations. In MBDC, the calculated wavenumbers at 2936, 2945, 2962, 2989, 2993, 2999, 3007, 3018 and 3101 cm\(^{-1}\) are assigned to C–H stretching modes which show good agreement with the literature values [18]. The C–H in-plane bending vibrations occur in the region of 1390–990 cm\(^{-1}\). The vibrational assignments at 900, 990 and 1000 cm\(^{-1}\) (Fig. 3) occur due to the effect of C–H in-plane bending vibrations. The calculated wavenumbers at 889, 903, 923, 951, 968, 992, 1011, 1029 and 1042 cm\(^{-1}\) are due to C–H in-plane bending vibrations which show good agreement with recorded spectral values.

The out-of-plane bending of ring C–H bonds occur below 900 cm\(^{-1}\) [19]. In MBDC, the C–H out-of-plane bending vibrations are observed at 540, 575, 600 and 725 cm\(^{-1}\) which are compared with the computed values at 527, 540, 572, 601, 633, 669, 689, 716 and 723 cm\(^{-1}\).

Carbon–carbon vibrations
The ring C=C and C–C stretching vibrations, known as semicircle stretching modes, usually occur in the region of 1625–1400 cm\(^{-1}\) [20]. Generally, these bands are of variable intensity and observed at 1625–1590 cm\(^{-1}\), 1590–1575 cm\(^{-1}\), 1540–1470 cm\(^{-1}\), 1465–1430 cm\(^{-1}\) and 1380–1280 cm\(^{-1}\) [21]. In MBDC, the aromatic C–C stretching vibrations are observed at 1209 cm\(^{-1}\) (Fig. 2). The C–C stretching vibrations are assigned at 1432 and 1500 cm\(^{-1}\) in FT-IR and at 1540 and 1600 cm\(^{-1}\) in FT-Raman spectrum. These values perfectly match with the calculated wavenumbers, 1306–1615 cm\(^{-1}\) (mode no: 64–78). The C–C=C in-plane bending vibrations are observed at 810 cm\(^{-1}\) in FT-IR spectrum and at 850 and 875 cm\(^{-1}\) in FT-Raman spectrum. The calculated values are 811–872 cm\(^{-1}\) (mode no: 33–40). The C–C=C out-of-plane bending vibrations appeared at 350 and 400 cm\(^{-1}\) in FT-Raman spectrum and the corresponding calculated wavenumbers at 255–453 cm\(^{-1}\) (mode no: 11–18) show good agreement with the literature values [16]. These observed wavenumbers show that the substitutions in the benzene ring affect the ring modes of vibrations to a certain extent.

### Table 1 Optimized geometrical parameters of (3E)-3-(4-methylbenzylidene)-3,4-dihydro-2H-chromen-2-one at B3LYP/6-31 + (G,p) level of theory

| Bond length | Value (Å) | Expt.* | Bond angle | Value (°) | Expt.* |
|-------------|-----------|--------|------------|-----------|--------|
| C1–C2       | 1.411     | 1.407  | C2–C1–C6   | 117.36    | 118.8  |
| C1–C6       | 1.408     |        | C6–C1–C7   | 124.68    | 124.0  |
| C1–C7       | 1.464     | 1.456  | C1–C2–H31  | 121.38    | 120.2  |
| C2–C3       | 1.390     | 1.378  | C3–C2–H18  | 119.56    | 119.0  |
| C2–H18      | 1.086     | 0.950  | C2–C3–C4   | 121.06    | 121.5  |
| C3–C4       | 1.404     | 1.378  | C3–C4–C5   | 117.74    | 117.3  |
| C3–H19      | 1.087     | 0.990  | C3–C4–C20  | 120.92    | 120.3  |
| C4–C5       | 1.401     | 1.403  | C5–C6–H25  | 118.79    | 119.8  |
| C4–C20      | 1.509     | 1.499  | C1–C7–C8   | 130.11    | 131.9  |
| C5–C6       | 1.394     | 1.389  | C8–C7–H26  | 114.99    |        |
| C5–H24      | 1.087     | 0.990  | C7–C8–C13  | 115.44    | 116.8  |
| C6–H25      | 1.083     |        | C7–C8–C9   | 126.11    | 125.5  |
| C7–C8       | 1.355     |        | C8–C9–C10  | 112.38    |        |
| C7–H26      | 1.088     | 0.950  | C8–C9–H28  | 109.63    |        |
| C8–C9       | 1.511     |        | C8–C9–H29  | 108.74    |        |
| C8–C13      | 1.491     | 1.491  | H28–C9–H29 | 106.06    | 107.2  |
| C9–C10      | 1.509     |        | C9–C10–C11 | 119.35    |        |
| C9–H28      | 1.102     |        | C9–C10–C14 | 122.68    |        |
| C10–C11     | 1.394     |        | C10–C13–O27| 125.15    |        |
| C10–C14     | 1.400     |        | C10–C14–H30| 118.76    |        |
| C11–O12     | 1.387     |        | C12–C11–C17| 116.22    | 116.6  |
| C11–C17     | 1.395     |        | C9–C8–C13  | 118.44    | 118.96 |
| O12–C13     | 1.376     |        | C11–C10–C14| 117.93    |        |
| C13=O27     | 1.211     | 1.261  | C1–C7–H26  | 114.86    |        |
| C14–H30     | 1.087     |        | C1–C6–C5   | 120.92    | 120.7  |
| C15–C16     | 1.399     |        | C1–C6–H25  | 120.23    |        |
| C17–H33     | 1.084     |        | C2–C3–H19  | 119.40    | 119.8  |

* X-ray data from Refs. [14] and [15]

symmetry is given by \( \Gamma_{VB} = 6A' + 30A'' \). All the vibrations are active in both IR and Raman spectra. Vibrational assignments have been carried out from FT-IR (Fig. 2) and FT-Raman (Fig. 3) spectra. The theoretically predicted wavenumbers along with their PED values are presented in Table 2. The fundamental vibrational modes are also characterized by their PED. The calculated wavenumbers are in good agreement with experimental wavenumbers.
750 cm\(^{-1}\) in FT-IR matches with the theoretical value of 748 cm\(^{-1}\). In this molecule, the peak observed at 500 cm\(^{-1}\) in FT-Raman and 506 cm\(^{-1}\) in FT-IR are attributed to C–O out-of-plane bending vibrations. The C=O stretching vibration is generally observed at 1800–1600 cm\(^{-1}\) [23]. In MBDC, the C=O stretching is observed at 1616 cm\(^{-1}\) in FT-IR and at 1690 cm\(^{-1}\) in FT-Raman spectrum. This peak matches with the calculated value (1692 cm\(^{-1}\)).

**CH\(_2\) vibrations**

The asymmetric CH\(_2\) stretching vibrations are generally observed between 3000 and 2800 cm\(^{-1}\), while the symmetric stretch appears between 2900 and 2800 cm\(^{-1}\) [24]. In MBDC, the CH\(_2\) asymmetric and symmetric stretching vibrations are calculated at 2809 and 2801 cm\(^{-1}\) respectively. The asymmetric bending is calculated at 1243 cm\(^{-1}\). In FT-IR spectrum the symmetric bending vibration is observed at 1215 cm\(^{-1}\) and calculated at 1231 cm\(^{-1}\). The in-plane CH\(_2\) bending vibration is observed at 1000 cm\(^{-1}\) in FT-Raman spectrum and the calculated vibration is at 1053 cm\(^{-1}\). The out-of-plane CH\(_2\) bending vibration is calculated at 1061 cm\(^{-1}\). The above results suggest that the observed frequencies are in good agreement with calculated in-plane and out-of-plane modes.

**CH\(_3\) vibrations**

There are nine fundamental modes associated with each CH\(_3\) group. In aromatic compounds, the CH\(_3\) asymmetric and symmetric stretching vibrations are expected in the range of 2925–3000 cm\(^{-1}\) and 2905–2940 cm\(^{-1}\), respectively [25]. In CH\(_3\) antisymmetric stretching mode, two C–H bonds are expanding while the third one is
contracting. In symmetric stretching, all the three C–H bonds are expanding and contracting in-phase. In MBDC, the assigned vibrations at 2911, 2889 and 2863 cm$^{-1}$ represent asymmetric and symmetric CH$_3$ stretching vibrations [26]. The CH$_3$ symmetric bending vibrations are observed at 1250 cm$^{-1}$ in FT-Raman spectrum and calculated at 1250 cm$^{-1}$ which are in good agreement with experimental and theoretical vibrations. The CH$_3$ asymmetric bending vibrations are observed at 1261 cm$^{-1}$ and calculated at 1260 and 1287 cm$^{-1}$ match with the experimental values. The in-plane CH$_3$ bending vibration is assigned at 1075 cm$^{-1}$ in FT-Raman and calculated at 1072 cm$^{-1}$ in B3LYP and out-of-plane CH$_3$ bending vibration is observed at 1100 cm$^{-1}$ in FT-Raman and calculated at 1104 cm$^{-1}$. Predicted wave-numbers derived from B3LYP/6-31 + G(d,p) method synchronise well with those of the experimental observations.

HOMO–LUMO analysis

The most important orbitals in the molecule is the frontier molecular orbitals, called highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). These orbitals determine the way the molecule interacts with other species. The HOMO–LUMO energy gap of MBDC is shown in Fig. 4. The HOMO (−51.0539 kcal/mol) is located over the coumarin group and LUMO (−49.0962 kcal/mol) is located over the ring; the HOMO→LUMO transition implies the electron density transfer to ring benzylidene. The calculated self-consistent field (SCF) energy of MBDC is $-506,239.7545$ kcal/mol. The frontier orbital gap is found to be $E = -101.9576$ kcal/mol and this negative energy gap confirms the intramolecular charge transfer. This proves the non-linear optical (NLO) activity of the material [27]. A molecule with a small frontier molecular orbital is more polarizable and generally associated with high chemical reactivity, low kinetic stability termed as soft molecule [28]. The low value of frontier molecular orbital in MBDC makes it more reactive and less stable.

NBO analysis

Natural bond orbital (NBO) of the molecule explains the molecular wave function in terms of Lewis structures, charge, bond order, bond type, hybridization, resonance, donor–acceptor interactions, etc. NBO analysis has been performed on MBDC to elucidate the intramolecular, rehybridization and also the interaction which
Table 2 The observed FT-IR, FT-Raman and calculated frequencies (in cm$^{-1}$) using B3LYP/6-31 + G (d,p) along with their relative intensities, probable assignments, reduced mass and force constants of (3E)-3-(4-methylbenzylidene)-3,4-dihydro-2H-chromen-2-one

| Mode nos | Observed frequencies (cm$^{-1}$) | Calculated frequencies (cm$^{-1}$) | Reduced mass (amu) | Force constant (mdyn/Å) | IR intensity (km/mol) | Raman intensity (Å$^4$ amu$^{-1}$) | Vibrational assignments (PED%) |
|----------|---------------------------------|---------------------------------|------------------|------------------------|---------------------|-------------------------------|---------------------------------|
|          | FTIR Unscaled | FTIR Scaled | FT Raman Unscaled | FT Raman Scaled |                    |                        |                                  |
| 1        | 23 20 0.140 | 98862.0 | τ Ring (56), τ CH$_3$ (20) |
| 2        | 36 29 0.259 | 2839.0 | τ Ring (56), τ CH$_3$ (20) |
| 3        | 48 42 0.138 | 4698.0 | τ Ring (55), τ CH$_3$ (18) |
| 4        | 61 60 0.126 | 4758.0 | τ Ring (56), τ CH$_3$ (20) |
| 5        | 81 78 1.029 | 1382.0 | τ Ring (55), τ CH$_3$ (22) |
| 6        | 101 96 0.456 | 0906.0 | γ C=O (58), τ CH$_3$ (21) |
| 7        | 156 143 1.546 | 0321.0 | τ CH$_3$ (58) |
| 8        | 189 181 0.402 | 1098.0 | τ CH$_3$ (56), γ CH$_3$ (18) |
| 9        | 225 202 2.382 | 0235.0 | γ C=CH$_3$ (54), γ CH (18), γ CH$_3$ (22) |
| 10       | 252 237 1.529 | 0314.0 | γ CC (62), γ CH (20), γ CH$_3$ (10) |
| 11       | 274 255 1.403 | 0314.0 | γ CCC (60), γ CH (22), γ CH$_3$ (11) |
| 12       | 314 286 0.632 | 0065.0 | γ CCC (59), γ CH (18), γ CH$_3$ (10) |
| 13       | 327 309 1.339 | 0029.0 | γ CCC (58), γ CH (18), γ CH$_3$ (11) |
| 14       | 368 354 0.038 | 0119.0 | γ CCC (60), γ CH (22), γ CH$_3$ (12) |
| 15       | 409 400 1.104 | 0482.0 | γ CCC (62), γ CH (18), γ CH$_3$ (10) |
| 16       | 421 413 1.829 | 0326.0 | γ CCC (62), γ CH (20), γ CH$_3$ (10) |
| 17       | 444 437 3.120 | 0773.0 | γ CCC (62), γ CH (22), γ CH$_3$ (11) |
| 18       | 457 453 3.817 | 0144.0 | γ CCC (63), γ CH (18), γ CH$_3$ (12) |
| 19       | 490 479 24.603 | 0378.0 | βC=O (58), βCC (22), γ CO (10) |
| 20       | 524 506 12.486 | 0794.0 | γ C=O (54), γ CH$_3$ (23), γ CO (10) |
| 21       | 540 527 5.539 | 0239.0 | γ CH (58), γ CH$_3$ (22), γ CC (10) |
| 22       | 545 540 4.599 | 0033.0 | γ CH (58), γ CC (21), γ CH$_3$ (11) |
| 23       | 582 572 2.309 | 0138.0 | γ CH (58), γ CH (20), γ CC (11) |
| 24       | 639 601 7.519 | 0104.0 | γ CH (56), γ CC (20), γ CH$_3$ (10) |
| 25       | 650 633 0.662 | 0176.0 | γ CH (58), γ CC (18), γ CH$_3$ (11) |
| 26       | 693 669 4.947 | 0007.0 | γ CH (56), γ CH (18), γ CC (12) |
| 27       | 711 689 0.262 | 0116.0 | γ CH (56), γ CC (16) |
| 28       | 727 716 9.921 | 0085.0 | γ CH (56), γ CC (18) |
| 29       | 737 723 11.299 | 0128.0 | γ CH (58), γ CC (18) |
| 30       | 740 735 0.599 | 0184.0 | βC–CH$_3$ (60), βCH (23) |
| 31       | 768 748 62.541 | 0034.0 | βC=O (62), βCC (22) |
| 32       | 778 760 7.458 | 0587.0 | βCC (58), βCH (21), βCH$_3$ (10) |
| 33       | 829 811 37.872 | 0230.0 | βCCC (63), βCH (21), βCH$_3$ (12) |
| 34       | 851 824 0.813 | 0119.0 | βCCC (63), βCH (18), βCH$_3$ (11) |
| Mode nos | Observed frequencies (cm\(^{-1}\)) | Calculated frequencies (cm\(^{-1}\)) | Reduced mass (amu) | Force constant (mdyn/Å) | IR intensity (km/mol) | Raman intensity (Å\(^4\) amu\(^{-1}\)) | Vibrational assignments (PED%) |
|----------|----------------------------------|-------------------------------------|------------------|------------------------|----------------------|---------------------------------------------|-----------------------------|
| 35       | FTIR 858 FT Raman 830            | 3.739                               | 1.625            | 14.149                 | 0.099                | βCCC (62), βCH (20), βCH (10)               |
| 36       | FTIR 862 FT Raman 838            | 2.202                               | 0.964            | 0.532                  | 0.021                | βCCC (62), βCH (21), βCH (12)              |
| 37       | FTIR 876 FT Raman 850            | 1.962                               | 0.888            | 3.587                  | 0.019                | βCCC (56), βCH (18), βCH (10)              |
| 38       | FTIR 919 FT Raman 861            | 6.652                               | 3.314            | 11.953                 | 0.005                | βCCC (58), βCH (18), βCH (12)              |
| 39       | FTIR 947 FT Raman 869            | 1.572                               | 0.831            | 5.009                  | 0.006                | βCCC (56), βCH (16), βCH (11)              |
| 40       | FTIR 875 FT Raman 872            | 1.399                               | 0.751            | 11.534                 | 0.087                | βCCC (61), βCH (20), βCH (10)              |
| 41       | FTIR 970 FT Raman 889            | 1.579                               | 0.877            | 3.474                  | 0.037                | βCH (78), v CC (18)                         |
| 42       | FTIR 981 FT Raman 903            | 1.476                               | 0.837            | 5.332                  | 0.041                | βCH (76), v CC (16)                         |
| 43       | FTIR 984 FT Raman 923            | 1.377                               | 0.786            | 2.738                  | 0.015                | βCH (78), v CC (13)                         |
| 44       | FTIR 988 FT Raman 951            | 1.282                               | 0.738            | 0.051                  | 0.002                | βCH (66), v CC (16)                         |
| 45       | FTIR 1010 FT Raman 968           | 1.409                               | 0.848            | 2.809                  | 0.020                | βCH (66), v CC (20)                         |
| 46       | FTIR 1033 FT Raman 992           | 2.848                               | 1.794            | 2.530                  | 0.024                | βCH (70), v CC (18)                         |
| 47       | FTIR 1056 FT Raman 1011          | 2.122                               | 1.396            | 3.275                  | 0.029                | βCH (76), v CC (18)                         |
| 48       | FTIR 1068 FT Raman 1029          | 1.545                               | 1.024            | 11.399                 | 0.009                | βCH (78), v CC (17)                         |
| 49       | FTIR 1088 FT Raman 1042          | 4.259                               | 2.975            | 171.99                 | 0.044                | βCH (78), v CC (17)                         |
| 50       | FTIR 1133 FT Raman 1053          | 1.775                               | 1.344            | 19.980                 | 0.028                | βCH\(_3\)\_ipr (67), βCH (20)              |
| 51       | FTIR 1148 FT Raman 1061          | 1.367                               | 1.063            | 20.088                 | 0.016                | γ CH\(_3\)op (66), βCH (21)                |
| 52       | FTIR 1180 FT Raman 1072          | 1.113                               | 0.914            | 4.889                  | 0.005                | βCH\(_3\)ipr (65), βCC (30)                |
| 53       | FTIR 1190 FT Raman 1104          | 2.389                               | 1.994            | 564.050                | 3.029                | γ CH\(_3\)op (71), βCC (23)                |
| 54       | FTIR 1215 FT Raman 1153          | 1.274                               | 1.109            | 16.185                 | 0.042                | v CO (58), βCH (18), v CC (11)              |
| 55       | FTIR 1218 FT Raman 1190          | 1.580                               | 1.381            | 27.443                 | 0.044                | v CO (58), βCH (18), v CC (12)              |
| 56       | FTIR 1227 FT Raman 1197          | 2.167                               | 1.924            | 37.004                 | 1.290                | v C=C (82), βCH (14)                        |
| 57       | FTIR 1238 FT Raman 1209          | 2.485                               | 2.247            | 7.534                  | 0.045                | v CC (71), βCH (16), v CH\(_3\) (12)       |
| 58       | FTIR 1255 FT Raman 1217          | 2.115                               | 1.964            | 33.951                 | 0.021                | v C=C\(_3\) (50), βCH (20), βCC (12)       |
| 59       | FTIR 1258 FT Raman 1231          | 3.099                               | 2.893            | 219.799                | 0.044                | βCH\(_3\)b (66), βCC (22), βCH (11)        |
| 60       | FTIR 1288 FT Raman 1243          | 1.825                               | 1.785            | 19.982                 | 0.058                | βCH\(_3\)ab (70), βCC (20), βCH (10)       |
| 61       | FTIR 1340 FT Raman 1250          | 5.462                               | 5.782            | 49.937                 | 0.079                | βCH\(_3\)ab (71), βCC (23), βCH (11)       |
| 62       | FTIR 1342 FT Raman 1260          | 1.625                               | 1.727            | 2.543                  | 0.057                | βCH\(_3\)ab (66), βCH (17), v CC (10)      |
| 63       | FTIR 1349 FT Raman 1287          | 2.373                               | 2.544            | 13.033                 | 0.043                | βCH\(_3\)ab (60), βCH (18), v CC (10)      |
| 64       | FTIR 1369 FT Raman 1306          | 2.450                               | 2.709            | 31.517                 | 0.047                | v CC (68), βCH (18)                         |
| 65       | FTIR 1407 FT Raman 1330          | 1.776                               | 2.074            | 9.480                  | 0.014                | v CC (66), βCH (19)                         |
| 66       | FTIR 1420 FT Raman 1343          | 1.248                               | 1.483            | 0.324                  | 0.039                | v CC (66), βCH (18)                         |
| 67       | FTIR 1440 FT Raman 1362          | 2.310                               | 2.850            | 7.463                  | 0.008                | v CC (68), βCH (19)                         |
| 68       | FTIR 1476 FT Raman 1387          | 1.277                               | 1.449            | 12.963                 | 0.009                | v CC (68), βCH (19)                         |
| 69       | FTIR 1491 FT Raman 1395          | 1.072                               | 1.450            | 11.786                 | 0.012                | v CC (70), βCH (18)                         |
| Mode nos | FTIR | FT Raman | Calculated frequencies (cm\(^{-1}\)) | Reduced mass (amu) | Force constant (mdyn/Å) | IR intensity (km/mol) | Raman intensity (Å\(^4\) amu\(^{-1}\)) | Vibrational assignments (PED%) |
|----------|------|----------|--------------------------------------|-------------------|------------------------|---------------------|-------------------------------|-------------------------------|
|          |      |          | Reduced mass (amu) |                  |                        |                     |                               |                                |
|          |      |          | FTIR Unscaled | FT Raman Unscaled | FTIR Scaled | FT Raman Scaled | FTIR Unscaled | FT Raman Unscaled | FTIR Scaled | FT Raman Scaled | FTIR Unscaled | FT Raman Unscaled | FTIR Scaled | FT Raman Scaled | FTIR Unscaled | FT Raman Unscaled | FTIR Scaled | FT Raman Scaled | FTIR Unscaled | FT Raman Unscaled | FTIR Scaled | FT Raman Scaled |
| 70       | 1492 | 1404     | 2.295                  | 3013             | 30.676               | 0.013               | v CC (70), βCH (1.7) |
| 71       | 1432 |          | 1.114                  | 1469             | 9.704               | 0.119               | v CC (68), βCH (1.7) |
| 72       | 1529 | 1487     | 2.593                  | 3574             | 57.049               | 0.019               | v CC (66), βCH (1.8) |
| 73       | 1548 | 1502     | 2.482                  | 3505             | 23.043               | 0.262               | v CC (65), βCH (1.8) |
| 74       | 1540 | 1543     | 5.415                  | 8200             | 5.106               | 0.0867              | v CC (66), βCH (1.9) |
| 75       | 1636 | 1587     | 6.310                  | 9958             | 21.097               | 0.0660              | v CC (65), βCH (1.8) |
| 76       | 1654 | 1592     | 6.049                  | 9754             | 145.323              | 0.3229              | v CC (66), βCH (1.8) |
| 77       | 1659 | 1604     | 6.840                  | 11109            | 9.718                | 0.093               | v CC (66), βCH (1.8) |
| 78       | 1668 | 1615     | 7.222                  | 11846            | 91.204               | 0.131               | v CC (70), βCH (1.6) |
| 79       | 1616 | 1692     | 12.541                 | 23775            | 370.738              | 0.0460              | v C=O (72), v CC (14) |
| 80       | 1690 | 2980     | 1.072                  | 5615             | 14.012               | 0.0299              | v ssCH\(_2\) (80) |
| 81       | 2800 | 3034     | 1.039                  | 5641             | 33.955               | 0.0722              | v assCH\(_2\) (82) |
| 82       | 3080 | 2863     | 1.088                  | 6085             | 4.273                | 0.0081              | v ssCH\(_3\) (72), v CH (23) |
| 83       | 3092 | 2889     | 1.097                  | 6182             | 17.402               | 0.0180              | v assCH\(_3\) (80), v CH (16) |
| 84       | 3122 | 2911     | 1.102                  | 6330             | 15.019               | 0.0127              | v assCH\(_3\) (88), v CH (11) |
| 85       | 3172 | 2936     | 1.088                  | 6451             | 3.815                | 0.0088              | v CH (96) |
| 86       | 3175 | 2945     | 1.088                  | 6464             | 5.999                | 0.0065              | v CH (96) |
| 87       | 3177 | 2962     | 1.088                  | 6464             | 7012                 | 0.0109              | v CH (96) |
| 88       | 3179 | 2989     | 1.089                  | 6488             | 17.412               | 0.0127              | v CH (98) |
| 89       | 3192 | 2993     | 1.089                  | 6536             | 7.580                | 0.0129              | v CH (98) |
| 90       | 3193 | 2999     | 1.094                  | 6574             | 14.859               | 0.0219              | v CH (96) |
| 91       | 3206 | 3007     | 1.094                  | 6629             | 18.471               | 0.0243              | v CH (98) |
| 92       | 3020 | 3218     | 1.096                  | 6687             | 5.949                | 0.0335              | v CH (98) |
| 93       | 3100 | 3225     | 1.091                  | 6690             | 6.782                | 0.0076              | v CH (98) |

v, stretching; β, in plane bending; γ, out of plane bending; ω, wagging; τ, torsion; ρ, rocking; δ, scissoring; ss, symmetric stretching; as, antisymmetric stretching; sb, symmetric bending; asb, antisymmetric bending; ipr, in plane-rocking; opr, out-of plane rocking
will weaken the bond associated with the anti-bonding orbital. Conversely, an interaction with a bonding pair will strengthen the bond.

The corresponding results are presented in Tables 3 and 4. The intramolecular interaction between lone pair of O27 with antibonding C13–O12 results in a stabilized energy of 35.64 kcal/mol. The most important interaction in MBDC is between the LP(2)O12 and the antibonding C13–O27. This results in a stabilization energy 41.74 kcal/mol and denotes larger delocalization. The valence hybrid analysis of NBO shows that the region of electron density distribution mainly influences the polarity of the compound. The maximum electron density on the oxygen atom is responsible for the polarity of the molecule. The p-character of oxygen lone pair orbital LP(2) O27 and LP(2) O12 are 99.66 and 99.88, respectively. Thus, a very close pure p-type lone pair orbital participates in the electron donation in the compound.

**Mulliken charges**

The Mulliken atomic charges of MBDC were calculated by B3LYP/6–31 + G(d,p) level theory (Table 5). It is important to mention that the atoms C1, C2, C4, C7, C10, H18, H19, O27 of MBDC exhibit positive charges, whereas the atoms C3, C5, C6, C11, O12 exhibit negative charges. The maximum negative and positive charge values are \(-0.95788\) for C11 and \(0.90500\) for C10 in the molecule, respectively.

**UV-Visible analysis**

Theoretical UV–Visible spectrum (Table 6) of MBDC was derived by employing polarizable continuum model (PCM) and TD-DFT method with B3LYP/6-31 + G(d,p) basis set and compared with experimentally obtained UV–Visible spectrum (Fig. 5). The spectrum shows the peaks at 215 and 283 nm whereas the calculated absorption maxima values are noted at 223, 265 and 296 nm in the solvent of ethanol. These bands correspond to one electron excitation from HOMO–LUMO. The band at 223 and 265 nm are assigned to the dipole-allowed \(\sigma \rightarrow \sigma^*\) and \(\pi \rightarrow \pi^*\) transitions, respectively. The strong transitions are observed at 2.414 eV (215 nm) with \(f = 0.0036\) and at 2.268 eV (283 nm) with \(f = 0.002\).

**Molecular electrostatic potential**

Molecular electrostatic potential at the surface are represented by different colours (inset in Fig. 5). Red
colour indicates electronegative character responsible for electrophilic attack, blue colour indicates positive region representing nucleophilic attack and green colour represents the zero potential. The electrostatic potential increases in the order red < orange < yellow < green < blue [29]. The mapped electrostatic potential surface of the molecule shows that atoms O27 and O12 of chromen possess negative potential and all H atoms have positive potential. The same regions are identified in the Mulliken charges also.

**Hyper polarizability**

On the basis of the finite-field approach, using B3LYP/6-31 + G (d,p) basis set, the first hyperpolarizability (β), dipole moment (μ) and polarizability (α) for MBDC are calculated and compared with urea (Table 7) [30]. The dipole moment of MBDC is 1.6941 times greater than the magnitude of urea (μtot of urea = 3.2705 D) and the first hyperpolarizability is 1.51 times greater than the magnitude of urea (βtot of urea = 3.7472 × 10−31 esu). Urea is the standard NLO crystal reported earlier [31] so that a direct comparison was made.

**Dielectric studies**

The experimental data of ε_0, ε′, ε_∞ and τ of MBDC in ethanol at various concentrations are presented in Table 8. The static and microwave dielectric constants decrease with increasing concentration of the compound. This shows a weak interaction exists between the molecule and the solvent at low frequencies. Optical dielectric constant increases with increasing solute concentration which leading to a strong interaction between MBDC and ethanol at high frequency. It indicates the formation of a hydrogen bonding between –OH group of alcohol and C=O of coumarin. The relaxation time increases with the increase of bond length confirming the degree of cooperation, shape and size of the molecule [32].

**NMR study**

The characterization of MBDC was further enhanced by the study of 1H NMR method. The computed 13C NMR and 1H NMR chemical shifts and experimental 1H NMR are compiled in Table 9. The experimental 1H NMR spectrum in CDCl3 solution is shown in Fig. 6. The relevant difference of 1H NMR chemical shifts calculated
by GIAO/B3LYP method is: 0.06(H31), 0.17(H26) and 0.19(H24). The maximum deviation from experimental value is responded to be 0.19 ppm for H24 atom [33]. Overall the calculated values agree with the experimental chemical shift values and the slight deviations may be due to the influence of proton exchange, hydrogen bond and solvent effect in complex real systems. The results of 13C NMR chemical shift of the MBDC compound is reliable for the interpretation of spectroscopic parameters. The C1 and C2 atoms of the compound are attached with the electron releasing group and hence they are more electron donating than C15. This causes more shielding at C1 and C2 positions and hence the chemical shift values are lesser.

**Molecular docking studies**

Glide docking was used to study the binding orientations and affinities of MBDC with tankyrase as target protein (Fig. 7). Tankyrases are ADP-ribosyltransferases that play key roles in various cellular pathways, including the regulation of cell proliferation, and thus they are promising drug targets for the treatment of cancer [12]. The keto atom in MBDC interacts with SER1068 and GLY1032 at distances of 3.17 and 2.91 Å, respectively (Table 10). This

---

**Table 4 NBO results showing the formation of Lewis and non Lewis orbitals of MBDC molecule by B3LYP/6-31G + (d,p) method**

| Bond (A–B) | ED/energy (a.u.) | ED_{A} % | ED_{B} % | NBO     | s %  | p %  |
|------------|------------------|----------|----------|---------|------|------|
| σ C8–C9    | 1.97667          | 50.31    | 49.69    | 0.7093  | 67.02| 32.98|
|            | −0.65200         |          |          | 0.7049  | 72.98| 27.02|
| σ C8–C13   | 1.97727          | 51.86    | 48.14    | 0.7201  | 71.27| 28.73|
|            | −0.68595         |          |          | 0.6938  | 60.28| 39.72|
| σ C9–H28   | 1.96228          | 63.78    | 36.22    | 0.7986  | 76.91| 23.09|
|            | −0.51190         |          |          | 0.6019  | 99.95| 0.05 |
| σ C10–C14  | 1.97139          | 51.60    | 48.40    | 0.7184  | 64.50| 35.50|
|            | −0.70409         |          |          | 0.6957  | 65.59| 34.41|
| σ C11–C17  | 1.97581          | 51.16    | 48.84    | 0.7153  | 61.80| 38.20|
|            | −0.71570         |          |          | 0.6989  | 66.64| 33.36|
| σ H30–C14  | 1.98112          | 37.66    | 62.34    | 0.6137  | 99.95| 0.05 |
|            | −0.53074         |          |          | 0.7896  | 70.31| 29.69|
| σ C17–C16  | 1.97651          | 50.46    | 49.54    | 0.7103  | 64.11| 35.89|
|            | −0.25929         |          |          | 0.7039  | 65.20| 34.80|
| σ C17–H33  | 1.97906          | 63.18    | 36.78    | 0.7948  | 69.15| 30.85|
|            | −0.52986         |          |          | 0.6068  | 0.04 | 99.96|
| σ C7–H26   | 1.96715          | 63.87    | 36.13    | 0.7992  | 72.22| 27.78|
|            | −0.52611         |          |          | 0.6011  | 0.05 | 99.95|
| σ C2–H18   | 1.98162          | 62.58    | 37.42    | 0.7911  | 70.02| 29.98|
|            | −0.52927         |          |          | 0.6117  | 99.95| 0.05 |
| σ C6–H25   | 1.98170          | 62.53    | 37.47    | 0.7908  | 70.03| 29.97|
|            | −0.53031         |          |          | 0.6121  | 99.95| 0.05 |
| σ C5–H24   | 1.98119          | 62.30    | 37.70    | 0.7893  | 70.34| 29.66|
|            | −0.52761         |          |          | 0.6140  | 99.95| 0.05 |
| σ C20–H21  | 1.98750          | 62.42    | 37.58    | 0.7901  | 75.70| 24.30|
|            | −0.51049         |          |          | 0.6130  | 0.05 | 99.95|
| LP(1) O27  | 1.97789          |          |          | sp^{0.00} | 58.63| 41.37|
|            | −0.69724         |          |          | sp^{0.00} | 99.95| 0.05 |
| LP(2) O27  | 1.83804          |          |          | sp^{0.00} | 00.05| 99.66|
|            | −0.26311         |          |          | sp^{0.00} | 34.56| 65.44|
| LP(1) O12  | 1.95794          |          |          | sp^{0.00} | 99.95| 0.05 |
|            | −0.54749         |          |          | sp^{0.00} | 00.00| 99.88|
result suggests that the MBDC binds well in the active site pocket of tankyrase and interact with the amino acid residues. These results are compared with the anti cancer drug molecule warfarin derivative. This drug molecule fits in the active site and favourable interactions are observed with the same residues. The results obtained reveals that both the molecules have comparable interactions and better docking scores.

Table 5: The charge distribution calculated by the Mulliken method

| Atoms | Mulliken charge | NBO |
|-------|----------------|-----|
| C1    | 0.35122        | -0.09783 |
| C2    | 0.07866        | -0.22079 |
| C3    | -0.25976       | -0.23196 |
| C4    | 0.28427        | -0.03843 |
| C5    | -0.54829       | -0.23334 |
| C6    | -0.26856       | -0.22441 |
| C7    | 0.10817        | -0.12331 |
| C8    | 0.48781        | -0.15456 |
| C9    | -0.49756       | -0.50908 |
| C10   | 0.90500        | -0.08766 |
| C11   | -0.95788       | 0.29617 |
| O12   | -0.39388       | -0.51439 |
| C13   | 0.33449        | 0.80701 |
| C14   | -0.31967       | -0.21966 |
| C15   | 0.13614        | -0.25219 |
| C16   | -0.08232       | -0.23483 |
| C17   | -0.15764       | -0.26075 |
| H18   | 0.13200        | 0.24986 |
| H19   | 0.12586        | 0.24422 |
| C20   | -0.60604       | -0.70947 |
| H21   | 0.17095        | 0.24897 |
| H22   | 0.16101        | 0.24929 |
| H23   | 0.15358        | 0.25629 |
| H24   | 0.12235        | 0.24404 |
| H25   | 0.12453        | 0.24877 |
| H26   | 0.15765        | 0.27521 |
| O27   | -0.44633       | -0.56839 |
| H28   | 0.18552        | 0.27671 |
| H29   | 0.16406        | 0.27813 |
| H30   | 0.12443        | 0.24480 |
| H31   | 0.12660        | 0.24891 |
| H32   | 0.13021        | 0.25025 |
| H33   | 0.14289        | 0.26243 |

Table 6: UV-Vis excitation energy and electronic absorption spectra of MBDC using TD-B3LYP/631G + (d,p) method

| Exp. (nm) | Wavelength (nm) | Energy (eV) | Oscillator strength (f) | Assignments |
|-----------|-----------------|-------------|-------------------------|--------------|
| 283       | 296             | 2.2007      | 0.0134                  | \(\pi \rightarrow \pi^*\) |
| 283       | 265             | 2.2684      | 0.002                   | \(\pi \rightarrow \pi^*\) |
| 215       | 223             | 2.4147      | 0.0036                  | \(\sigma \rightarrow \sigma^*\) |

Table 7: The calculated electric dipole moment (\(\mu_{\text{tot}}\) D), the average polarizability (\(\alpha_{\text{tot}} \times 10^{-24}\) esu) and the first hyperpolarizability (\(\beta_{\text{tot}} \times 10^{-31}\) esu)

| Parameters          | Values          |
|---------------------|-----------------|
| \(\mu_x\)           | 2.9237          |
| \(\mu_y\)           | -4.6995         |
| \(\mu_z\)           | -0.2541         |
| \(\mu_{\text{tot}}\) (D) | 5.5406         |
| \(\alpha_{xx}\)     | -93.6767        |
| \(\alpha_{xy}\)     | 6.1433          |
| \(\alpha_{yz}\)     | -119.8535       |
| \(\alpha_{zz}\)     | -0.1725         |
| \(\alpha_{\text{tot}}\) (esu) | 2.32632 \times 10^{-24} |
| \(\beta_{xx}\)      | 23.1945         |
| \(\beta_{xy}\)      | -28.7842        |
| \(\beta_{yy}\)      | 20.1351         |
| \(\beta_{zz}\)      | -51.2342        |
| \(\beta_{\text{tot}}\) (esu) | 6.4779         |
| \(\beta_{\text{tot}}\) (esu) | 5.6583 \times 10^{-31} |
Anticancer activity

The results of the antiproliferative activity of MBDC and Warfarin derivative against MCF-7 breast cancer and HT-29 colon cancer cell lines at different concentrations (7.8, 15.6, 31.2, 62.5, 125, 250, 500 and 1000 μg/ml) for 24 h, and cell proliferation was measured by a standard MTT assay. As shown in Figs. 8a, b and 9a, b, MCF-7 and HT-29 cells exposed to MBDC and Warfarin derivative exhibited significant cytotoxicity in the dose dependent manner after 24 h treatment. The estimated half maximal inhibitory concentration (IC₅₀) value for MBDC and Warfarin derivative was 15.6 and 31.2 μg/ml respectively. This enhanced cytotoxicity of MBDC in MCF-7 breast cancer and HT-29 colon cancer cell lines may be due to their efficient targeted binding and eventual uptake by the cells.

Conclusion

The vibrational and molecular structure analysis have been performed based on the quantum mechanical approach using DFT calculations. The difference in the observed and scaled wavenumber values of most fundamentals is very small. Therefore, the assignments made using DFT theory with experimental values seem to be correct. The geometrical structure shows a little distortion due to the substitution of methyl benzylidene and chromen group in the benzene.

The chromen group substitution plays an important role with its characteristic peaks compared in both experimental and theoretical FTIR and FT-Raman spectra. The MEP map shows negative potential sites on O27 and O12 of chromen and positive potential sites on all H atoms which are responsible for electrophilic and nucleophilic attacks, respectively.
In addition, HOMO and LUMO orbitals are in agreement with MEP. The results indicate that the title compound is found to be useful to bond metallicity and intermolecular interaction. The NBO analysis explains the large delocalization of charge in the molecule. The predicted NLO properties are compared with that of urea and the title compound seems to be a good candidate of second-order NLO materials.

Molecular docking study shows that MBDC binds well in the active site of tankyrase and interact with the amino acid residues. These results are compared with the anti-cancer drug molecule of warfarin derivative. The results suggest that both the molecules have comparable interactions and better docking scores. The results of the anti-proliferative activity of MBDC and Warfarin derivative against MCF-7 breast cancer and HT-29 colon cancer
cell lines at different concentrations exhibited significant cytotoxicity. The estimated half maximal inhibitory concentration (IC \(_50\)) value for MBDC and Warfarin derivative was 15.6 and 31.2 \(\mu\)g/ml, respectively. This enhanced cytotoxicity of MBDC in MCF-7 breast cancer and HT-29 colon cancer cell lines may be due to their efficient targeted binding and eventual uptake by the cells. Hence the compound MBDC may be considered as a
Table 10 Hydrogen bond interactions of title compound and co-crystal ligand with amino acids at the active site of tankyrases

| Docking score | Glide energy (kcal/mol) | Hydrogen bonding interactions | Donor | Acceptor | Distance (Å) |
|---------------|-------------------------|-------------------------------|-------|----------|--------------|
| MBDC          |                         |                               |       |          |              |
| −10.823       | −49.845                 | N–H[GLY1032]                 | O     |          | 2.91         |
|               |                         | O–H[SER1068]                 | O     |          | 3.17         |
| Warfarin      |                         |                               |       |          |              |
| −10.625       | −55.759                 | NH[Tyr1060]                  | O     |          | 2.0          |
|               |                         | NH[Gly1032]                  | O     |          | 2.1          |
|               |                         | OH                           | O(Gly1032) | 2.0 |
|               |                         | OH                           | N[His1031] | 3.7 |
|               |                         | N[His1048]                  | O     |          | 3.3          |

Fig. 8 Graphical representation of MBDC molecule on a MCF-7 cell line and b HT-29 cell line
drug molecule for cancer. The dielectric relaxation studies show the existence of molecular interactions between MBDC and alcohol. The NMR spectrum confirms the molecular structure of the compound.

**Authors’ contributions**

TB proposed the work, carried out the DFT studies, dielectric, NMR and anticancer studies, arranged the results and drafted the manuscript under the guidance of LS. Spectroscopic studies carried out by AN under the guidance of VB. DK synthesized the title compound. Molecular docking, manuscript revision and final shape were done by MNP. All authors read and approved the final manuscript.

**Acknowledgements**

MNP thanks UGC, New Delhi for the financial support in the form of UGC-Emeritus Fellowship. We wish to thank (BIF) at CAS in Crystallography and Biophysics, University of Madras, Guindy Campus, Chennai-25.

**Competing interests**

This is the characterization study which provides the needed information to prove that the molecule MBDC competes with Warfarin derivative as an anticancer agent.

**Received:** 9 May 2016  **Accepted:** 7 December 2016  
**Published online:** 10 January 2017
References

1. Madari H, Panda D, Wilson L, Jacobs RS (2003) Dicoumarol: a unique microtubule stabilizing natural product that is synergistic with Taxol. Cancer Res 63:1214–1220
2. Takeuchi Y, Xie L, Cosentino LM, Lee HK (1997) Anti-AIDS agents—XXVIII. Synthesis and anti-HIV activity of methoxy substituted 3′,4′-di-O-(−)-camphanoyl-(+) cis-khellactone (DCK) analogues. Bioorg Med Chem Lett 7:2573–2578
3. Manolov I, Moessmer CM, Danchev N (2006) Synthesis, structure, toxicological and pharmacological investigations of 4-hydroxycoumarin derivatives. Eur J Med Chem 41:882–890
4. Ostrov DA, Prada JA, Consino PE, Finton KA, Le N, Rowe TC (2007) Discovery of novel DNA gyrase inhibitors by high-throughput virtual screening. Antimicrob Agents Chemother 51:3688–3698
5. Koshy L, Dwarakanath BS, Raj HG, Chandra R, Mathew TL (2007) Suicidal oxidative stress induced by certain antioxidants Indian. J Exp Biol 41:1273–1278
6. Ghate M, Manohar D, Kulkarni V, Shobha R, Kattimani SY (2003) Synthesis of vanillin ethers from 4-((bromomethyl) coumarins as anti-inflammatory agents. Eur J Med Chem 38:297–302
7. Baba M, Jin Y, Mizuno A, Suzuki H, Okada Y, Takasuka N, Tokuda H, Nishino H, Okuyama T (2002) Studies on cancer chemoprevention by traditional folk medicines XIX, Inhibitory effect of a coumarin derivative, 7-nopentenylcoumarin, against tumor-promotion. Biol Pharm Bull 25:244–246
8. Gacche RN, Jadhav SG (2012) Antioxidant activities and cytotoxicity of selected coumarin derivatives: preliminary results of a structure–activity relationship study using computational tools. J Exp Clin Med 4:165–169
9. Paramjeet KM, Dipak S, Arti D (2012) Overview of synthesis and activity of coumarins. Int Sci Res J 4:16–37
10. Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE et al (2009) Gaussian, Inc., Wallingford
11. Frisch A, Nielsen AB, Holder AJ (2007) Gaussview users manual. Gaussian Inc., Pittsburgh
12. Nawal M, Koivunen J, Haikarainen T, Obaji E, Ongey E, Venkannagari LH, Joensuu P, Pihlajaniemi T, Lehtiö L (2013) Discovery of tankyrase inhibiting flavones with increased potency and isoenzyme selectivity. J Med Chem 56:7880–7889
13. Varsanyi G (1969) Vibration spectra of benzene derivatives. Akademiai Kiado, Budapest
14. Coates J (2000) Interpretation of infrared spectra a practical approach. In: Meyers RA (ed) Encyclopedia of analytical chemistry. Wiley, Chichester
15. Vein DL, Colthup NB, Fateley WG, Grasselli JG (1991) The handbook of infrared and Raman characteristic frequencies of organic molecules. Academic Press, New Delhi
16. Matulkova I, Nemec I, Teubner K, Nemec P, Micka Z (2008) Novel compounds of 4-amino-1,2,4-triazole with dicarboxylic acids—crystal structures, vibrational spectra and non-linear optical properties. J Mol Struct 873:46–60
17. Colthup NB, Daly LH, Wiberly SE (1990) Introduction of infrared and Raman spectroscopy, 3rd edn. Academic Press, New York
18. Sunndaraganan S, Elango G, Sebastian S, Subramani P (2009) Molecular structure, vibrational spectroscopic studies and analysis of 2-fluoro-5-methylbenzonitrile. Indian J Pure Appl Phys 47:481–490
19. Handy NC, Masien PE, AMos RD, Andrews JS, Munro CW, Laming G (1992) The harmonic frequencies of benzene. Chem Phys Lett 197:506–515
20. Powell BJ, Baruah T, Bernstein N, Brake K, McKenzie RH, Meredith P, Pederson MR (2004) A first-principles density-functional calculation of the electronic and vibrational structure of the key melanin monomers. J Chem Phys 120:8608–8615
21. Thul P, Gupta VP, Ram JV, Tandon P (2010) Structural and spectroscopic studies on 2-pyranones. Spectrochim Acta A Mol Biomol Spectrosc 75:251–258
22. Sun YX, Hao QL, Wei WX, Yu ZX, Lu LD, Wang X, Wang YS (2009) Experimental and density functional studies on 4-(3,4-dihydroxybenzylideneamino) antipyrine, and 4-(2,3,4-trihydroxybenzylideneamino) antipyrine. J Mol Struct THEOCHEM 904:74–82
23. Reis H, Papadopoulos MG, Munn RW (1998) Calculation of macroscopic first-, second-, and third-order optical susceptibilities for the urea crystal. J Chem Phys 109:6628–6838
24. Dharmalingam K, Ramachandran K, Sivagurunathan P (2007) Hydrogen bonding interaction between acrylic esters and monohydric alcohols in non-polar solvents: an FTIR study. Spectrochim Acta A Mol Biomol Spectrosc 66:48–51
25. Osmałowicz B, Kolehmainen E, Gawańcki R (2001) GIAO/DFT calculated chemical shifts of tautomeric species. 2-Phenacylpyridines and (Z)-2-(2-hydroxy-2-phenylvinyl)pyridines. Magn Reson Chem 39:334–340