Figure 27A depicts the H&E staining analysis of liver and kidney samples from a tissue distribution study in nude mice administered a single dose of 10 mg/kg by weight of Compound I.

Figure 27B depicts the results of tissue distribution studies from 0.5 h to 96 h in the heart, lungs, muscles, spleen, tibia, and femur of nude mice administered a single dose of 10 mg/kg by weight of Compound I.

Figures 28A-28E are graphs showing the effect on the organ weight (Figure 28A-28B), liver weight (Figure 28C), and body weight (Figure 28D-28E) of male and female Wistar rats upon oral administration of various amounts of Compound I.

Figures 28F-28I are graphs showing the effect on haematological parameters (urea, creatinine, etc.) when male and female Wistar rats are orally administered various amounts of Compound I.

Figures 28J-28K are graphs showing the effect on electrolytes when male and female Wistar rats are orally administered various amounts of Compound I.

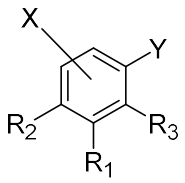
Figures 28L-28O are graphs showing the effect on liver function of male and female Wistar rats upon oral administration of various amounts of Compound I.

Figures 28P-28Q are graphs showing the effect on kidney function of male and female mice upon oral administration of various amounts of Compound I.

Figures 29A-29B depict histopathological studies from the analysis of the organ samples of liver, kidney, skeletal muscle, heart, and spleen from both male (Figure 29A) and female rats (Figure 29B). Tissue samples were collected on the final day of the treatment period.

SUMMARY

The present disclosure is related to compounds with anticancer and antiviral activity. The compounds may be used for treating subjects with chronic disorder. The compounds have a structure in of Formula 1A



Formula 1A

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

in which:

R_1 is H, OH, or alkoxy;

R_2 is alkoxy, or OH;

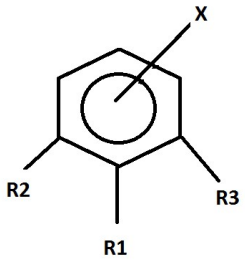
R_3 is alkoxy or OH;

X is C_1-C_{15} alkyl, C_2-C_{15} alkenyl, C_2-C_{15} alkynyl, or aralkyl chain, each of which is independently substituted with at least one alkoxy, OH, =NH , or oxo, group;

Y is H or alkyl; and

X is in ortho position to R_2, or para position to R_1.

In an aspect of the present disclosure, there is provided a compound of Formula 1



Formula 1

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

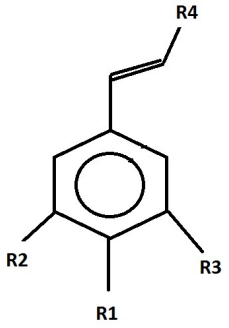
R_1 is H, alkoxy, or OH;

R_2 is alkoxy or OH;

R_3 is alkoxy or OH;

X is C_1-C_{15} alkyl, C_2-C_{15} alkenyl, or aralkyl, each of which is independently substituted with at least one alkoxy, OH, =NH, or oxo group.

In another aspect of the present disclosure, there is provided a compound of Formula 2



Formula 2

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

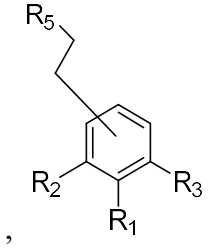
R_1 is H or OH;

R_2 is alkoxy or OH;

R_3 is alkoxy or OH; and

R_4 is an C_1-C_{15} alkyl, C_2-C_{15} alkenyl, or aralkyl, each of which is substituted with at least one alkoxy, -OH, or oxo.

In a further aspect of the present disclosure, there is provided a compound of Formula 3



,

Formula 3

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

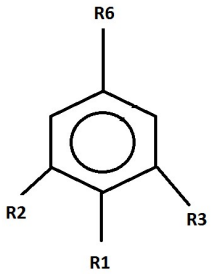
R_1 is H, alkoxy, or OH;

R_2 is alkoxy or OH;

R_3 is alkoxy or OH; and

R_5 is C_1-C_{12}alkyl or C_2-C_{12} alkenyl, which is independently substituted with 1, or 2, substituents selected from the group consisting of =NH and oxo.

In another aspect of the present disclosure, there is provided a compound of Formula 4;



Formula 4

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

R_1 is OH;

R_2 is C_1-C_3 alkoxy;

R_3 is C_1-C_3 alkoxy; and

R_6 is $C(CH_2)OH$.

In another aspect of the present disclosure, there is provided a pharmaceutical composition, comprising a compound disclosed herein and a pharmaceutically acceptable carrier.

In a further aspect of the present disclosure, there is provided a use of a compound disclosed herein or a pharmaceutical composition disclosed herein, in the manufacture of a medicament for treating a chronic disorder in a patient in need thereof.

In another aspect of the present disclosure, there is provided a compound disclosed herein or a pharmaceutical composition disclosed herein, for use in therapy.

DETAILED DESCRIPTION OF THE INVENTION

Definitions

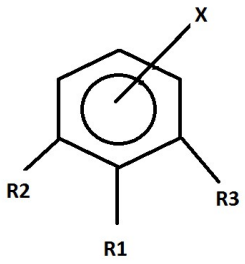
"Alkyl" or "alkyl group" refers to a fully saturated, straight or branched hydrocarbon chain having from one to fifteen carbon atoms, and which is attached to the rest of the molecule by a single bond. Unless stated otherwise specifically in the specification, an alkyl group can be optionally substituted.

"Alkenyl" or "alkenyl group" refers to a straight or branched hydrocarbon chain having from two to fifteen carbon atoms, and having one or more carbon-carbon double bonds. Each alkenyl group is attached to the rest of the molecule by a single bond. Unless stated otherwise specifically in the specification, an alkylene chain can be optionally substituted.

"Alkenylene" or "alkenylene chain" refers to a straight or branched divalent hydrocarbon chain radical, having from two to twelve carbon atoms, and having one or more carbon-carbon double

WE CLAIM:

1. A compound of Formula 1



Formula 1

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

R_1 is H, alkoxy, or OH;

R_2 is alkoxy or OH;

R_3 is alkoxy or OH;

X is C_1-C_{15} alkyl, C_2-C_{15} alkenyl, or aralkyl, each of which is independently substituted with at least one alkoxy, OH, =NH, or oxo group.

2. The compound as claimed in claim 1 wherein X is:

(i) C_6-C_{10} alkenyl, substituted with four substituents independently selected from the group consisting of oxo, -OH, and C_1-C_3 alkoxy;

(ii) C_8-C_{12} alkenyl substituted with oxo and C_1-C_3 alkoxy;

(iii) C_4-C_8 alkenyl substituted with two oxo groups;

(iv) C_2-C_6 alkenyl substituted with oxo and C_1-C_3 alkoxy;

(v) C_1-C_6 alkyl substituted with =NH;

(vi) C_2-C_3 alkenyl substituted with –OH;

(vii) C_8-C_{12} alkenyl substituted with oxo and 2 C_1-C_3 alkoxy groups; and

(viii) aralkyl comprising a C_6-C_8 alkyl and a C_6 aryl, wherein the alkyl is substituted with oxo and the aryl is substituted with two alkoxy groups.

3. The compound as claimed in claim 2, wherein:
R_1 is H;
R_2 is C_1-C_3 alkoxy;
R_3 is C_1-C_3 alkoxy; and
X is C_6-C_{10} alkenyl, substituted with oxo, -OH, and two C_1-C_3 alkoxy groups.

4. The compound as claimed in claim 2 , wherein
R_1 is H;
R_2 is C_1-C_3 alkoxy;
R_3 is C_1-C_3 alkoxy; and
X is C_8-C_{12} alkenyl substituted with oxo and C_1-C_3 alkoxy.

5. The compound as claimed in claim 2 , wherein
R_1 is OH;
R_2 is C_1-C_3 alkoxy;
R_3 is C_1-C_3 alkoxy; and
X is C_4-C_8 alkenyl substituted with two oxo groups.

6. The compound as claimed in claim 2, wherein
R_1 is C_1-C_3 alkoxy;
R_2 is OH;
R_3 is C_1-C_3 alkoxy; and
X is C_4-C_8 alkenyl substituted with two oxo groups.

7. The compound as claimed in claim 2, wherein
R_1 is H;
R_2 is OH;
R_3 is OH; and

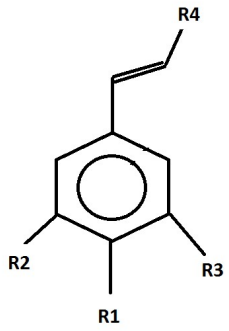
X is C_1-C_6 alkyl substituted with =NH.

8. The compound as claimed in claim 2, wherein
R_1 is OH;
R_2 is C_1-C_3 alkoxy;
R_3 is C_1-C_3 alkoxy; and
X is C_2-C_3 alkenyl substituted with OH.

9. The compound as claimed in claim 2, wherein
R_1 is H;
R_2 is C_1-C_3 alkoxy;
R_3 is C_1-C_3 alkoxy; and
X is C_8-C_{12} alkenyl substituted with oxo and 2 C_1-C_3 alkoxy groups.

10. The compound as claimed in claim 2, wherein
R_1 is OH;
R_2 is C_1-C_3 alkoxy;
R_3 is C_1-C_3 alkoxy; and
X is aralkyl comprising a C_6-C_8 alkyl and a C_6 aryl, wherein the alkyl is substituted with oxo and the aryl is substituted with two C_1-C_3 alkoxy groups.

11. A compound of Formula 2



Formula 2

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

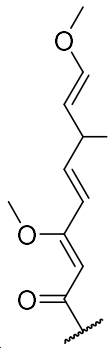
R_1 is H or OH;

R_2 is alkoxy or OH;

R_3 is alkoxy or OH; and

R_4 is an C_1-C_{15} alkyl, C_2-C_{15} alkenyl, or aralkyl, each of which is substituted with at least one alkoxy, -OH, or oxo.

12. The compound as claimed in claims 11, wherein R_4 is selected from the group consisting of: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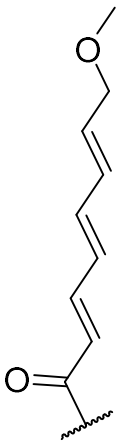
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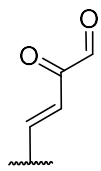
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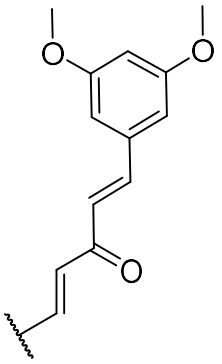
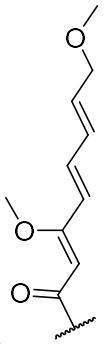
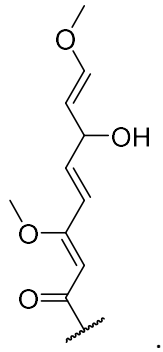

, and


13. The compound as claimed in claim 11, wherein

R_1 is H;

R_2 is OCH_3;

R_3 is OCH_3; and

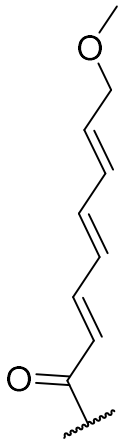
R_4 is  .

14. The compound as claimed in claim 11, wherein

R_1 is H;

R_2 is OCH_3;

R_3 is OCH_3; and

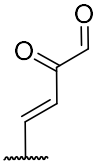
R_4 is. 

15. The compound as claimed in claim 11, wherein

R_1 is OH;

R_2 is OCH_3;

R_3 is OCH_3; and

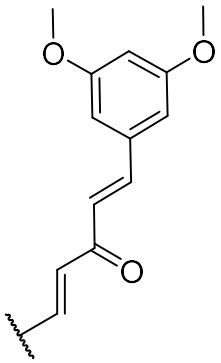
R_4 is  .

16. The compound as claimed in claim 11, wherein

R_1 is OH;

R_2 is OCH_3;

R_3 is OCH_3; and

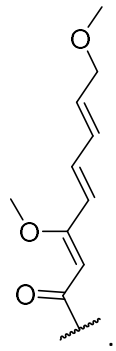
R_4 is  .

17. The compound as claimed in claim 11, wherein

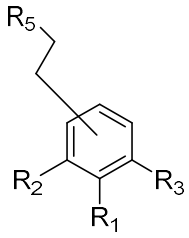
R_1 is H;

R_2 is OCH_3;

R_3 is OCH_3; and

R_4 is  .

18. A compound of Formula 3



,

Formula 3

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

R_1 is H, alkoxy, or OH;

R_2 is alkoxy or OH;

R_3 is alkoxy or OH; and

R_5 is C_1-C_{12}alkyl or C_2-C_{12} alkenyl, which is independently substituted with 1, or 2, substituents selected from the group consisting of =NH and oxo.

19. The compound as claimed in claim 18, wherein

R_1 is H;

R_2 is OH;

R_3 is OH; and

R_5 is =NH, wherein

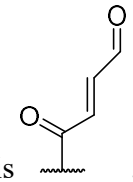
R_5 is in the ortho position to R_2.

20. The compound as claimed in claim 18, wherein

R_1 is $–OC_2H_5$;

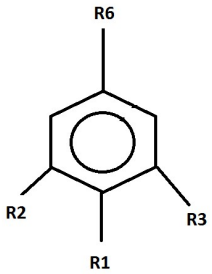
R_2 is OH;

R_3 is $–OCH_3$;

R_5 is  , wherein

R_5 is in the para position to R_1.

21. A compound of Formula 4;



Formula 4

or any derivative thereof, pharmaceutically acceptable salt thereof, or combination thereof

wherein:

R_1 is OH;

R_2 is C_1-C_3 alkoxy;

R_3 is C_1-C_3 alkoxy; and

R_6 is $C(CH_2)OH$.

22. The compound as claimed in claim 21, wherein

R_1 is OH;

R_2 is OCH_3;

R_3 is OCH_3; and

R_6 is $C(CH_2)OH$.

23. A pharmaceutical composition, comprising a compound of one of claims 1-22 and a pharmaceutically acceptable carrier.

24. Use of a compound of claims 1-22 or a pharmaceutical composition of claim 23, in the manufacture of a medicament for treating a chronic disorder in a patient in need thereof.

25. The use as claimed in claim 24, wherein the chronic disorder is acute lymphoblastic, acute lymphoblastic leukemia, acute lymphocytic leukemia, acute myelogenous leukemia, acute myeloid leukemia, adrenocortical carcinoma, AIDS -related lymphoma, anal cancer, appendix cancer, basal-cell carcinoma, bladder cancer, brain cancer, brainstem glioma, breast cancer, bronchial adenomas/carcinoids, Burkitt's lymphoma, carcinoid tumor, cerebellar or cerebral astrocytoma, cervical cancer, cholangiocarcinoma, chondrosarcoma, chronic lymphocytic or chronic lymphocytic leukemia, chronic myelogenous or chronic myeloid leukemia, chronic myeloproliferative disorders, colon cancer, cutaneous T-cell lymphoma, desmoplastic small round cell tumor, endometrial uterine cancer, ependymoma, esophageal cancer, Ewing's sarcoma, extracranial germ cell tumor, extragonadal germ cell tumor, extrahepatic bile duct cancer, gallbladder cancer, gastric

(stomach) cancer, gastrointestinal carcinoid tumor, gastrointestinal stromal tumor (GIST), gestational trophoblastic tumor, glioma of the brain stem, hairy cell leukemia, head and neck cancer, heart cancer, hepatocellular (liver) cancer, Hodgkin lymphoma, hypopharyngeal cancer, hypothalamic and visual pathway glioma, intraocular melanoma, Islet cell carcinoma, Kaposi sarcoma, laryngeal cancer, leukaemia, lip and oral cavity cancer, liposarcoma, lymphoma, male breast cancer, malignant mesothelioma, medulloblastoma, melanoma, Merkel cell skin carcinoma, mesothelioma, metastatic squamous neck cancer, mouth cancer, multiple endocrine neoplasia syndrome, multiple myeloma, multiple myeloma/plasma cell neoplasm, mycosis fungoides, myelodysplastic/myeloproliferative diseases, nasal cavity and paranasal sinus cancer, nasopharyngeal carcinoma, neuroblastoma, non-Hodgkin lymphoma, non-melanoma skin cancer, non- small cell lung cancer, oligodendroglioma, oral cancer, oropharyngeal cancer, osteosarcoma and malignant fibrous histiocytoma, ovarian cancer, ovarian germ cell tumor, ovarian epithelial cancer (surface epithelial- stromal tumor), ovarian low malignant potential tumor, pancreatic cancer, paranasal sinus and nasal cavity cancer, parathyroid cancer, penile cancer, pharyngeal cancer, pheochromocytoma, pineal astrocytoma, pineal germinoma, pineoblastoma and supratentorial primitive neuroectodermal tumors, pituitary adenoma, plasma cell neoplasia, pleuropulmonaryblastoma, primary carcinoma, primary central nervous system lymphoma, primary liver cancer, prostate cancer, rectal cancer, renal cell carcinoma, renal pelvis and ureter carcinoma, retinoblastoma, rhabdomyosarcoma, salivary gland cancer, Sezary syndrome, small cell lung cancer, small intestine cancer, soft tissue sarcoma, squamous cell carcinoma, stomach cancer, supratentorial primitive neuroectodermal tumor, testicular cancer, throat cancer, thymoma and thymic carcinoma, thyroid cancer, transitional cell cancer of the renal pelvis and ureter, urethral cancer, uterine sarcoma, vaginal cancer, visual pathway and hypothalamic glioma, vulvar cancer, Waldenstrom macroglobulinemia, Wilms tumor, Parkinson's disease and Parkinsonian disorders, Huntington's disease, Alzheimer's disease, multiple sclerosis, amyotrophic lateral sclerosis, Shy-Drager syndrome, progressive supranuclear palsy, Lewy body disease, spinal ischemia, spinal cord injuries, ischemic stroke, cerebral infarction, spinal cord injury, and cancer-related brain and spinal cord injury, multi-infarct dementia, geriatric dementia, other cognitive impairments, depression, Onychomycosis (fungal

infection of the nail, Gingivitis and Periodontal Disease (Gum Disease) obesity, diabetes, a viral infection, or KRAS oncogene mutated cancer.

26. The use as claimed in claim 24, in which the chronic disorder is cancer.

27. The use as claimed in claim 26, in which the cancer is colon cancer, prostate cancer, breast cancer, or leukemia.

28. The use as claimed in claim 26, in which the cancer has a KRAS oncogene mutation.

29. The use as claimed in claim 24, in which chronic disorder is a viral infection.

30. The use as claimed in claim 29, in which the viral infection is SARS or COVID-19.

31. The use as claimed in any one of claims 26-28, wherein the compound or the pharmaceutical composition is to be administered to the patient, and wherein a chemotherapeutic agent is to be further administered to the patient in need thereof .

32. The use as claimed in claim 31, in which the chemotherapeutic agent is selected from the group consisting of docetaxel, paclitaxel, pazobanib, endoxon, etoposide, adriamycin, dacromycin, avastin, gemcitabine, cisplatin and oxaliplatin.

33. The use as claimed in claim 31 or 32, in which the compound or the pharmaceutical composition reduces and/or reverses the toxic side effects associated with the chemotherapeutic agent.

34. The use of claim 33, in which the toxic side effects associated with the chemotherapeutic agent include one or more of gastritis, hair loss, bone marrow suppression, and cardiac toxicity.

35. The use as claimed in claim 29 or 30, wherein an additional antiviral agent is to be further administered to the patient in need thereof.

36. The use as claimed in claim 34, in which the additional antiviral agent is chloroquine or hydroxychloroquine.

37. The use as claimed in claim 35, in which the compound or the pharmaceutical composition reduces and/or reverses the toxic side effects associated with the chloroquine or hydroxychloroquine.

38. The use of claim 36, in which the toxic side effects associated with the chloroquine or hydroxychloroquine include one or more of cardiovascular diseases, eye damage, mild or severe bronchospasm, and mental health conditions.

39. A compound of claims 1-22, or a pharmaceutical composition of claim 23, for use in therapy.