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Phytochemical investigation of *Solidago Canadensis L.* and its activity against Colorectal Adenocarcinoma and acute monocytic leukemia

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***Abstract*---**Due to the increase in cancer cases worldwide, natural products are gaining interest, particularlythose herb-based extractsare growing. Plants are classified as one of the primary suppliers of bioactive components. The species *Solidago Canadensis,* Asterales, Asteraceae, and Plantae are found in Iraq. The upper parts of these plants are very often utilized to treat inflammatory disorders. *S. Canadensis L.* has been extracted as phytochemical compounds for anti-colorectal adenocarcinoma and -acute monocytic leukemia (AML) in in-vivo cancer models to find novel sources of the anticancer mixture.The relationship between each investigation is one of the critical phases for the effects associated with this particular style of study. In the present research, extracted phytochemical compounds from *S. Canadensis L.* were discovered to significantly inhibit colorectal adenocarcinoma and AML in vitro, and the narrative makes this compound promising for antitumor activity testing in vivo.

***Keywords*---**colorectal adenocarcinoma, phytochemicals, *Solidago Canadensis*, acute monocytic leukemia.

1. Introduction

Cancer is regarded as a serious public health issue because it is the leading cause of morbidity and mortality worldwide(1).Cancer treatment is generally defined as a combination of surgery, tumor removal, chemotherapy, immunotherapy, and radiation(2,3). Nevertheless, most malignancies continue to exhibit moderate responses to therapeutic regimens, reducing the

appropriateness, and effective treatments for primary tumors and metastasis(4). The efficiency of carcinoma medications is frequently hampered by their poor solubility and stability, the slow percentage that the tissues absorb, as well as tumor medicationresistance(5). Furthermore, many antineoplastic drugs are associated with an increase in adverse-effect percentage, which leads to toxicity(6). Therefore, many of the negative effects associated with currently offered chemotherapeutic medicines motivate the exploration of novel, highly effective, and easily absorbed medications.Pharmacological investigations with plant extracts and substituted analogs among those herbal extracts have indeed been increased in an attempt to produce more efficient and safer outcomes(7,8).

Herbal medicines were considered a useful source of effective therapeutic medicines, with the development of various bioactive bio-active molecules, tuned to perform biological tasks (9). Plant phytochemicals, such as polyphenols, flavanols, and oil, have been discovered to influence cancer tumor tissue, affecting reductions of between 30% and 40% of tumors (10). *Solidago canadensis L.* contains phytochemicals, such as phenolics, flavonoids, and essential oils, which play an important part in the control agents β-thujone and Limonene(11). *Solidago*, sometimes known as *goldenrods*, is a species of between 110-119 plant species in the *Asteraceae* family (12). Herbal compounds are a good source of anticancer drugs that are both safe and effective, and they often lead to the development of new medicines (13). Many plant species in the Asteraceae family can be used to treat such as cancer, inflammation, and infections(14). Phytochemicals extracted from natural plant sources have always had the potential to improve the efficacy of ovarian anticancer therapy while somehow contributing to the mitigation of the negative consequences of ovarian cancer. Uche et al. (15). recently discovered that phytochemicals extracted from plants and their derivatives, which are used in the analysis of ovarian tumors, have a major effect on the reduction in ovarian cancer cells.In South America, the aerial sections of *S. Canadensis L.* have been used for burn therapy due to their healing properties and as antirheumatic, anti-inflammatory, analgesic, and diuretic(16,17). Based on chemical tests, the ethanolic phytochemical compounds extract from the aerial sections of *S. Canadensis L.*havemany types of terpenes and terpenoids like phytol, bornyl acetate, andrographolide, elemol, caryophyllene oxide, and others (18–20). The present study aimed to examine the anticancer activity of *S. Canadensis L.* and its phytochemical extract, which are considered a strong alternative to medicinal chemicals because they are natural sources.

2. Materials and Methods

All reagents and solvents used, except as noted, were of analytical reagent quality. Gas chromatography-mass spectrometry (GC–MS) grade was used for GC–MS analysis. The chemicals were obtained from Riedel-de Haen, Germany.

2.1. Plant material

Prof. Dr. SukaenaAbass, Department of Biology, College of Sciences, University of Baghdad, verified the plant material. The aerial section of *S. Canadensis* was obtained in Iraq, Babylon City, in October of 2020.First, the aerial sections were washed and then dried at room temperature (25°C). A centrifugal mill was used to

grind materials into a fine powder. The sample's fine flour was kept at 4 °C in a plastic container before extraction.

2.2. Extraction and preparation of phytochemicals

Phytochemical extraction was carried out by the cold method of extraction in which a Fine powder of *S. Canadensis*(750 g)was macerated for 24 hours with hexane as a solvent (21)Afterwards, the sample was filtered under vacuum and evaporated to drynessusing a rotary evaporator (Heidolph Germany Rotavapor), and the dried sample 2.7gm was stored in a refrigerator at 2 ℃ for further biological evaluation.

2.3. Preliminary qualitative phytochemical analysis of crude extracts

Analysis of Phytochemical compounds in the aerial sections of *S. Canadensis L.* was conducted according to Harborne (1998)(22).

2.4. Test for terpenoids

Five ml of the sample, 2 mL of chloroform, and 3 mL of H_2SO_4 were mixed. A layer of reddish-brown coloration was formed at the interface, indicating a positive result for the presence of terpenoids. At the interface, a layer of reddish-brown coloration appeared, suggesting a good result for the presence of terpenoids.

2.5. Gas chromatography-mass spectrometry (GC-MS) analysis of essential oils

Essential oils were analyzed using GC–MS (QP2020, Tokyo, Japan)in accordance withAlfekaik and AL-Hilfi(23). the profile of GC–MS was equipped with an Rtx-1MS-fused bonded column (30 m × 0.25 mm i.d. × 0.25 µm film thickness, Restek, USA) and a split–splitless injector. The first-column temperature was retained at 45 °C for 2 min (isothermal) before being programmed to 300 °C at a rate of 5 °C/min for 5 min (isothermal). The temperature of the injector was 250 °C. The flow rate of helium carrier gas was 1.41 mL/min. The following parameters were used to obtain all of the mass spectra: (equipment current) 60 mA filament emission current, 70 eV ionization voltage, 200 °C, and ion-source split mode used to inject diluted samples (1 percent v/v, a split ratio of 1:15). A Shimadzu QP2010 quadrupole was used for the GC–MS analysis of the hexane extract. A carbowax (30 m 0.25 mm ID; 0.25 m film thickness) capillary column was used in the GC–MS apparatus (Intercut DB5MS, Japan). One µl of the sample was injected into the column. Helium was used as the carrier gas. Injector and detector temperatures were set at 280 °C. The injection was performed in split mode (1:30). The column temperature was determined to be 50 °C at first, and then it was increased at the rate stated in Table 1 until it reached a final temperature of 280 °C. Peaks were found by comparing mass spectra to the mass spectral database while the chemicals were separated at constant pressure (100 kPa). The compounds were identified by comparing their mass spectra to those in the NIST Library.

Cell culture of colorectal adenocarcinoma

Nawah Scientific Inc (Mokatam, Cairo, Egypt) supplied colorectal adenocarcinoma. Cells of colorectal adenocarcinoma were incubated in Dulbecco's Modified Eagle Medium (DMEM) enriched with 10% of heat-inactivated fetal bovine serum in humidified, 100 units/mL of penicillin, 100 mg/mL of streptomycin and 5% (v/v) CO2 atmosphere at 37 °C.

Cytotoxicity assay of colorectal adenocarcinoma

The WST-1 test (ab155902 WST-1 Cell Proliferation Reagent)has been used to evaluate the vitality of colorectal cancer cells. 50 µL cell suspension (3×10^3 cells) sample arrangement in the plates after that incubated with media for a 1 day, and then the colorectal adenocarcinoma cells were provided treatment with different concentrations of the 50 µL media containing extracted phytochemical compounds (EPCs) at serial concentrations (0.01, 0.1, 1, 10, and 100µg/mL, DMSO as solvent) for 48 h. Afterward, they have been treated with a 10 µL WST-1 reagent. Finally, using a BMG LABTECH- FLUOstar Omega microplate reader(Allmendgrün, Ortenberg), the absorbance was measured at 450 nm after 60 minutes.

Cell culture of Anti-acute monocytic leukemia

Anti-acute monocytic leukemia was obtained from Nawah Scientific Company (Mokatam, Cairo, Egypt). The Anti-acute monocytic leukemia cell keeps remaining in RPMI media, enriched with 10% of heat-inactivated fetal bovine serum in humidified, 100 units/mL of penicillin, 100 mg/mL of streptomycin, and 5% (v/v) CO_2 atmosphere at 37 °C.

Cytotoxicity assay of Anti-acute monocytic leukemia

The WST-1 test (ab155902 WST-1 Cell Proliferation Reagent)has been used to evaluate the vitality of colorectal cancer cells. 50 µL cell suspension (3×10^3 cells) sample arrangement in the plates after that incubated with media for a 1 day, and then the colorectal adenocarcinoma cells were provided treatment with different concentrations of the 50 µL media containing extracted phytochemical compounds (EPCs) at serial concentrations (0.01, 0.1, 1, 10, and 100µg/mL, DMSO as solvent) for 48 h. Afterward, they have been treated with a 10 µL WST-1 reagent. Finally, using a BMG LABTECH- FLUOstar Omega microplate reader (Allmendgrün, Ortenberg), the absorbance was measured at 450 nm after 60 minutes.

3. Results and Discussion

3.1. Phytochemicals compounds of *S. Canadensis L.*

The occurrence of phytochemical compounds was shown through GC–MS analysis of *S. Canadensis L.* phytochemical compounds. Table 2 shows the phytochemical compounds together with their molecular weight, molecular

formula, retention time, compound nature, and area (100%).The aqua-ethanol (85%) extract of *S. Canadensis L.* is an unique mixture of several ingredients, and GC–MS detected 51 compounds of *S. Canadensis L.* Phytochemical compounds, such as bornyl acetate (0.15%), andrographolide (0.36%), Z,Z,Z-1,4,6,9-nonadecatetraene (0.65%), trans-chrysanthemal (0.25%), 1-oxaspiro[2.5]octane (34%), andrographolide (1%), 4,7,10,13,16,19-docosahexaenoic acid, methyl ester, (all-Z)(0.86%),11,11-dimethyl-spiro [2,9]dodeca-3,7-dien (0.46%), cyclohexanemethanol, 4-ethenyl-.alpha.,.alpha., elemol (1.08%), doconexent (1.12%), caryophyllene oxide (3.42%), cis-lanceol (2.4%), 1,3-bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one (0.32%), dactylol (0.32%), β-cembrenediol (1.11%), cyclopentaneacetaldehyde (1.2%), bicyclo [6.1.0] nonane (0.75%), 8,11,14-eicosatrienoic acid, methyl ester (0.36%), 2H, benzocyclohepten-2-one (1.13%), 1H-2,8a-methanocyclopenta, [a]cyclopropa[e]cyclodecen-11-one (6.85%), cyclopropa[d]naphthalen-3-one, octahydro (0.37%), 2,4a,8,8-tetramethyl-, oxime (0.37%), phthalic acid, isobutyl tridec-2 yn-1-yl ester (0.83%), aromadendrene oxide-(2) (5.04%), kauran-18-al, 17-(acetyloxy)-, (4.beta.) (2.16%), dichloroacetic acid, tridec-2-ynyl ester (1.04%), 13,1, octadecadiynoic acid, methyl ester (1.95%), caryophyllene oxide (0.62%), 1-methyl-6-(3-methylbuta-1,3-dienyl)-7-oxabicyclo [4.1.0]heptane (0.41%), pentadecanoic acid (5.5%) and 7,10-hexadecadienoic acid, methyl ester (0.60%), 7-hexadecenoic acid, methyl ester, (Z) (1.43%), phytol (10.04%), hexadecanoic acid, 15-methyl-, methyl ester (0.23%), cyclohexanol, 2-methylene-5-(1-methylethenyl) (0.72%), 3-tetradecyn-1-ol (12.68%), octadecanoic acid, stearic acid (0.98%), (2Z)-3-pentyl-2,4-pentadien-1-ol (1.07%), 2-methyl-3-isopropenylcyclohexanol (0.73%), (2E,6E)-3,7-dimethyl-2,6-nonadienyl acetate (4.12%), cyclobutane carboxylic acid, tridec-2-ynyl ester (0.50%) and 1,6-dibromo-2-cyclohexylpentane (8.47%), 1,1-propanedicarbonitrile 1,2-dicyclohexyl-(4.23%), (2E,6E)-3,7,11-trimethyl-2,6-dodecadien-1-ol (1.44%), 2-butenoic acid, 2-methyl-, dodecahydro-8-hydroxy-8a-methyl-3,5, bis(methylene)-2-oxonaphtho[2,3-b]furan-4-yl ester (0.35%), 2,3,3-trimethyl-1,7-octadiene (0.52%), 3-methyl-2-butenoic acid, dodec-9-ynyl ester (0.49%), methyl 12-oxo-9-dodecenoate (3.37%), butane-1,1-dicarbonitrile, 1-cyclohexyl-3-methyl (1.10%), cyclohexane, (2-nitro-2-propenyl) (2.03%), butane-1,1-dicarbonitrile, 1-cyclohexyl-3-methyl (1.20%) were determined in *S. Canadensis L.* ethanol extract by referring to the appropriate peak region with the use of associated GC–MS as shown Fig. 1. Several reports have shown that these phytochemicals are found in *S. Canadensis L.* and that the extracted phytochemical of *S. Canadensis L.* contain various types of important phytochemical compounds(24–26), which have a major role on the anticancer, anti-arthritis, anti-inflammatory, antigout, antiviral, antimicrobial, and antioxidant effects (10,27–31). In the present study, phytol, 1,6-dibromo-2-cyclohexylpentane, [a]cyclopropa[e]cyclodecen-11-one, pentadecanoic acid, aromadendrene oxide-(2), 1,1-propanedicarbonitrile 1,2-dicyclohexyl, cyclohexane, andrographolide, cyclohexanemethanol, 4-ethenyl-.alpha.,.alpha., elemol and doconexent, and kauran-18-al, 17-(acetyloxy)-, (4.beta.) showed higher ratios than other phytochemical compounds by (10.04%), (8.47%), (6.85%), (5.5%), 5.04%, (4.23%), (2.03%), 1.36%, 1.08%, 1.12%, and 2.16%, respectively. According to our findings, andrographolide comprises 1.36 % of the phytochemical compounds detected in the *S. Canadensis L.* as well as, Zhang et al. (12) investigated the phytol concentration of*S.caesia, S.tortifolia, S.nemoralis,* and*S.rogsos*, which were detected at ratios of 21, 0.16, 0.10, and 0.15%, respectively. In this study, phytol was detected at a ratio of around 10.04 %,

which is a high ratio in the *S. Canadensis L*, especially compared to previous research. Many of the phytochemical compounds of *S. Canadensis L.* discovered were consistent with previous research (12,24,29,32,33).

3.2. Cytotoxicity

Natural ingredients derived from plants provide important promise for the production of innovative treatments(34). These components are identified as major suppliers of anticancer compounds (24). In addition, an estimated 60% of chemotherapeutic drugs are derived from natural sources, either directly or indirectly (8). In the present research, phytochemical compoundsof*S. Canadensis L.* were developed at various concentrations (0.01–100 µg/ml) with low and high molecular weight, identifying around 51 compounds in Table 2 and their chemical structure in Fig. 2 and 3. These findings supported those of previous research on the aerial parts of *S. Canadensis L.* basedon Gomes et al. (24), Wang et al.(25), and Mohamed et al. (26); and their possible mechanisms, including angiogenesis inhibition, differentiation, stimulation of cell death, cellular division inhibition, anti-proliferative effects, and carcinogen deactivation (35,36). Raffa et al. (36) reported that andrographolide plays a major role in the inhibition of NF-κB, JAK-STAT, PI3K, HSP90, and MMPs in the cancer cell. As illustrated in Fig. 6, the process and stages for inhibiting cancer cells following exposure to *S. Canadensis L.* EPCs. The findings in the present study showed that extracted phytochemicals have a high amount of phytol, 1,6-dibromo-2-cyclohexylpentane, [a]cyclopropa[e]cyclodecen-11-one, and andrographolide, representing clear evidence to the reduction in colorectal adenocarcinoma cell (Table 2). According to Choudhari et al. (37)reported that these compounds are naturally occurring physiologically and biological active ingredients with significant anticancer effects. As well, the phytol compound has a major role in the reduction of cancer cells Ajayi et al.(38), Kumar et al.(39); Shah et al. (40). As shown in Fig. 4, the EPC derived from *S. Canadensis L.* exhibited an effect on the reduced viability of acute monocytic leukemia at the concentration of 10 µg/mL. Furthermore, the viability of colorectal adenocarcinoma cells was affected at a concentration of 10 µg/mL and continuously decreased to reach 22% at a concentration of 100 µg/mL. According to Fouche et al. (41), in the National Cancer Institute (NCI) guidelines for in-vitro antiproliferative screening, extracts with total inhibition growth values of less than or equal to 50 g/mL are promising applicants. This criterion was carried out in the present study.

The EPC of *S. Canadensis L.* showed a promising antiproliferative effect against colorectal adenocarcinoma and acute monocytic leukemiacells, mainly because of the presence of more lipid biochemical contents in lower polarity extracts, leading to the efficient attraction of these compounds to cellular membranes (42). Diterpenes 6-tigloyloxyolavenic acid and 6-angeloyloxykolavenic acid extracted from *S. canadensis L.* inflorescences play a major role in the effect against hepatoma, tumor, colon cancer, leukemia, cervical cancer, and breast cancer (43). These compounds were identified in the extracted phytochemicals of *S. Canadensis L* (Table 2). Meanwhile, the intraperitoneal LD_{50} of the isolated phytochemical *S. Canadensis* has not been classified as a “harmless” molecule. As a result, the recovered phytochemical compounds are considered to have been from natural sources and are nontoxic.

Anticancer *S Canadensis L.*-derived phytochemicals

Phytochemicals generated from plants have the potential to improve the effectiveness of ovarian anticancer therapy while helping to reduce the detrimental effects of ovarian cancer (30,37). According to considerable in-vivo and in-vitro research, phytochemicals contain bioactive features that include active ingredients and their polyphenolic constituents, such as flavonoids, flavones, cancer prevention agents, and essential oils, and provide significant protection against various kinds of cancer (30,44).Several researchers have reported that many phytochemicals in the current investigation exhibit medicinal characteristics. For instance, andrographolide, elemol, and Phytol have been associated with a multitude of biological activities. Betulin, 1-heptatriacotanol, diol,2,3-dimethyl-5-trifluoromethyl, phen1,4- 1-ethynyl-3, trans(1,1-dimethylethyl)-4, 7-methyl-Z-tetradecen, O-α-D-glucopyranosyl-(1. Fwdarw.3)-β-dfructofuranosyl, α-D-glucopyranoside, and 6-ol pivalate showed antioxidant, anticancer, anti-inflammatory, anticarcinogenic, and antibiotic activities (45,46). Yu et al. (47) reported that andrographolide treatment plays a major role in anti-colon cancer by inhibiting the migration of Ras-transformed cells for colon cancer. According to our findings, andrographolide comprises 1.36 % of the phytochemical compounds detected in the *S. Canadensis L.* as well as, Zhang et al. (12) investigated the phytol concentration of *S.caesia, S.tortifolia, S.nemoralis,* and*S.rogsos*, which were detected at ratios of 21, 0.16, 0.10, and 0.15%, respectively. In this study, phytol was detected at a ratio of around 10.04 %, which is a high ratio in the *S. Canadensis L*, especially compared to previous research. According to Ajayi et al.(38), Kumar et al.(39), and Shah et al. (40), phytol extracts from plant sources are anti-cancer. Plant-derived medications are widely used for anticancer therapy because they are natural and easily obtainable.

3.3. Histopathological analysis

The biochemical findings were corroborated by the morphology of a normal colorectal adenocarcinoma, which showed typical clear colorectal adenocarcinoma cell viability (Fig. 5A). Severe accumulation and aggression were observed in cancer tissue after EPC treatment at a dose of 0.01 µg/mL (Fig. 5B). The colorectal adenocarcinoma treated with EPC (0.1 µg/mL) showed a loss of cells on the surface morphology of colorectal adenocarcinoma, as shown in Fig. 5C. Treatment with EPCs (10 and 100 µg/mL) increased the toxic manifestations in the colorectal adenocarcinoma cell and decreased the number of colorectal adenocarcinoma cells with the increase inthe dose of EPC (Figs. 5E and F). This finding is consistent with the findings in cell viability cytotoxicity in thecytotoxicity section. The present findings also suggested that the excess inEPCs resulted in a decrease in cell viability of acute monocytic leukemia and cytocolorectal adenocarcinoma activities compared with the normal control sample of cancer tissue. This decreasewas caused by increased lipid peroxidation or the inactivation of enzymes inthe cancer tissue (27). When the cancer tissue was treated with EPCs from plants, the cell viability of acute monocytic leukemia and colorectal adenocarcinoma cells was reduced, as shown in Fig. 5. The phytochemical compounds have a significant anticancer effect by inactivating the enzymes present in cancer tissue (10,26–28,30).

Conflicts of Interest
The authors confirm that they have no conflicting interests.

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Conclusion

The phytochemical components isolated from the aerial parts of *S. Canadensis* showed promising anticancer activity in vitro. The main phytochemicals found in theEPCs have a powerful antiproliferative effect on acute monocytic leukemia and cytocolorectal adenocarcinoma activity cell lines. The phytochemical extract of *S. Canadensis* exceeds the fundamental physicochemical parameters for absorption and bioavailability, and the demonstrated physiological activities are most likely due to the molecule's interaction with nuclear receptors and as an enzyme inhibitor.

References

1. Abdulhafiz F, Mohammed A, Kayat F, Bhaskar M, Hamzah Z, Podapati SK, et al. Xanthine oxidase inhibitory activity, chemical composition, antioxidant properties and GC-MS analysis of keladi candik (Alocasia longiloba Miq). Molecules. 2020;25(11).
2. Ajayi IA, Ajibade O, Oderinde RA. Preliminary Phytochemical Analysis of some Plant Seeds. Res J Chem Sci. 2011;1(3):5862.
3. Akindele AJ, Wani ZA, Sharma S, Mahajan G, Satti NK, Adeyemi OO, et al. In vitro and in vivo anticancer activity of root extracts of sansevieria liberica Gerome and labroy (Agavaceae). Evidence-based Complement Altern Med. 2015;2015.
4. AL-Hilfi DFAS. A. Fatty Acids Composition by (GC-MS) and Most Important physical chemicals parameters of seed oil pomegranate and grape seeds. J Biol Agric Healthc. 2016;6(8).
5. Assini FL, Fabrício EJ, Lang KL. Efeitos farmacológicos do extrato aquoso de Solidago chilensis Meyen em camundongos. Vol. 15, Revista Brasileira de Plantas Medicinais. 2013. p. 130–4.
6. Atanasov AG, Waltenberger B, Linder T, Wawrosch C, Uhrin P, Temml V, et al. Discovery and resupply of pharmacologically active plant-derived natural 2 products: a review. Biotechnol Adv [Internet]. 2015;33(8):1582–614. Available from: http://dx.doi.org/10.1016/j.biotechadv.2015.08.001
7. B.Gomes D et al. Antiproliferative potential of solidagenone isolated of Solidago chilensis. Brazilian J Pharmacogn. 2018;28(6).
8. Bao J-L, Chen X-P, Wang Y-T, Huang M, Huang M-Q, Lu J-J. Terpenoids: natural products for cancer therapy. Expert Opin Investig Drugs. 2012;21(12):1801–18.
9. Baskar R, , Kuo Ann Lee RY and K-WY. Cancer and Radiation Therapy: Current Advances and Future Directions. Int J Pharm Pharm Sci. 2012;9(3):193–9.
10. Chorawala, M.R. & Oza, Pratik & Shah G. Mechanisms of anticancer drugs resistance: an overview. J Pharm Technol Drug Res. 2012;1(1):1–9.

11. Choudhari AS, Mandave PC, Deshpande M, Ranjekar P, Prakash O. Phytochemicals in cancer treatment: From preclinical studies to clinical practice. Front Pharmacol. 2020;10.
12. Costa-Lotufo L V., Montenegro RC, Alves APNN, Madeira SVF, Pessoa C, Moraes MEA de, et al. The Contribution of Natural Products as Source of New Anticancer Drugs: Studies Carried Out at the National Experimental Oncology Laboratory from the Federal University of Ceará. Rev Virtual Química. 2010;2(1).
13. da Costa LS, Andreazza NL, Correa WR, Cunha IB da S, Ruiz ALTG, de Carvalho JE, et al. Antiproliferative activity, antioxidant capacity and chemical composition of extracts from the leaves and stem of Chresta sphaerocephala. Rev Bras Farmacogn. 2015;25(4):369–74.
14. Dawood Shah M, Seelan Sathiya Seelan J, Iqbal M. Phytochemical investigation and antioxidant activities of methanol extract, methanol fractions and essential oil of Dillenia suffruticosa leaves. Arab J Chem. 2020;13(9):7170–82.
15. dos Santos LC, Álvarez-Rivera G, Sánchez-Martínez JD, Johner JCF, Barrales FM, de Oliveira AL, et al. Comparison of different extraction methods of Brazilian “pacová” (Renealmia Petasites Gagnep.) oilseeds for the determination of lipid and terpene composition, antioxidant capacity, and inhibitory effect on neurodegenerative enzymes. Food Chem X. 2021;12.
16. Fouche G, Cragg GM, Pillay P, Kolesnikova N, Maharaj VJ, Senabe J. In vitro anticancer screening of South African plants. J Ethnopharmacol. 2008;119(3):455–61.
17. Greenwell M, Rahman PKSM. Medicinal Plants: Their Use in Anticancer Treatment. Int J Pharm Sci Res. 2015;6(10):4103–12.
18. Grul’ová D, Pl’uchtová M, Fejér J, De Martino L, Caputo L, Sedlák V, et al. Influence of six essential oils on invasive Solidago canadensis L. seed germination. Nat Prod Res. 2020;34(22):3231–3.
19. Hadi MY, Mohammed GJ, Hameed IH. Analysis of bioactive chemical compounds of Nigella sativa using gas chromatography-mass spectrometry. J Pharmacogn Phyther. 2016;8(2):8–24.
20. Hameed IH, Hussein HJ, Kareem MA, Hamad NS. Identification of five newly described bioactive chemical compounds in Methanolic extract of Mentha Viridis by using gas chromatography-mass spectrometry (GC-MS). J Pharmacogn Phyther. 2015;7(7):107–25.
21. Harborne J. Phytochemical Methods A Guide to Modern Techniques of Plant Analysis. 1998. 320 p.
22. Hassig CA, Zeng FY, Kung P, Kiankarimi M, Kim S, Diaz PW, et al. Ultra-high-throughput screening of natural product extracts to identify proapoptotic inhibitors of Bcl-2 family proteins. J Biomol Screen. 2014;19(8):1201–11.
23. Hudaib MM, Tawaha KA, Mohammad MK, Assaf AM, Issa AY, Alali FQ, et al. Xanthine oxidase inhibitory activity of the methanolic extracts of selected Jordanian medicinal plants. Vol. 7, Pharmacognosy Magazine. 2011. p. 320–4.
24. Issinger OG, Guerra B. Phytochemicals in cancer and their effect on the PI3K/Akt-mediated cellular signaling. Biomed Pharmacother. 2021;139.

25. Kakde D, Jain D, Shrivastava V, Kakde R, Patil AT. Cancer therapeutics-opportunities, challenges, and advances in drug delivery. J Appl Pharm Sci. 2011;1(9):1–10.
26. Koh YC, Ho CT, Pan MH. Recent advances in cancer chemoprevention with phytochemicals. J Food Drug Anal. 2020;28(1):14–37.
27. Kumar B, Vijayakumar M, Govindarajan R, Pushpangadan P. Ethnopharmacological approaches to wound healing-Exploring medicinal plants of India. J Ethnopharmacol. 2007;114(2):103–13.
28. Lee CC, Houghton P. Cytotoxicity of plants from Malaysia and Thailand used traditionally to treat cancer. J Ethnopharmacol. 2005;100(3):237–43.
29. Li D, Pan S, Zhu X, Tan L, Cao Y. Anticancer activity and chemical composition of leaf essential oil from Solidago canadensis L. in China. Adv Mater Res. 2012;347–353:1584–9.
30. Lorenzini H, Matos FJA. Plantas medicinais do Brasil: nativas e exóticas. Inst Plant. 2002;642.
31. Mohamed Isa SSP, Ablat A, Mohamad J. The antioxidant and xanthine oxidase inhibitory activity of plumeria Rubra flowers. Molecules. 2018;23(2).
32. Newman DJ, Cragg GM. Natural Products as Sources of New Drugs from 1981 to 2014. J Nat Prod. 2016;79(3):629–61.
33. Newman DJ, Cragg GM. Natural products as sources of new drugs over the 30 years from 1981 to 2010. J Nat Prod. 2012;75(3):311–35.
34. Palani S, Raja S, Kumar R, Selvaraj R, Kumar BS. Evaluation of phytoconstituents and anti-nephrotoxic and antioxidant activities of Monochoria vaginalis. Pak J Pharm Sci. 2011;24(3):293–301.
35. Prakash O, Kumar A, Kumar P, Ajeet A. Anticancer Potential of Plants and Natural Products: A Review. Vol. 1, American Journal of Pharmacological Sciences. 2013. p. 104–15.
36. Pundir M, Sharma A, Kumar J. Phytochemicals used as inhibitors in the treatment of ovarian cancer: A Mini-review. Mater Today Proc. 2022;48(5):1620–5.
37. Radušienė J, Karpavičienė B, Marksa M, Ivanauskas L, Raudonė L. Distribution Patterns of Essential Oil Terpenes in Native and Invasive Solidago Species and Their Comparative Assessment. Plants. 2022;11(9).
38. Raffa D, Maggio B, Raimondi MV, Plescia F, Daidone G. Recent discoveries of anticancer flavonoids. Eur J Med Chem. Elsevier Masson SAS; 2017;142:213–28.
39. Rais J, Jafri A, Siddiqui S, Tripathi M, Arshad M. Phytochemicals in the treatment of ovarian cancer. Front Biosci. 2017;9(1):67–75.
40. Suryasa, I. W., Rodríguez-Gámez, M., & Koldoris, T. (2021). Get vaccinated when it is your turn and follow the local guidelines. International Journal of Health Sciences, 5(3), x-xv. https://doi.org/10.53730/ijhs.v5n3.2938
41. T. Hasan H, J. Kadhim E. Phytochemical Investigation of Corchorus olitorius L. Leaves Cultivated in Iraq and its In Vitro Antiviral Activity. Iraqi Journal of Pharmaceutical Sciences (P-ISSN: 1683 - 3597, E-ISSN : 2521 - 3512). 2018. p. 115–22.
42. Torres LMB, Roque NF, Akisue MK. Diterpenes from the roots of Solidago microglossa. Rev Latinoamer Quim. 1989;20:94–7.
43. Uche FI, Abed MN, Abdullah MI, Drijfhout FP, McCullagh J, Claridge TWD, et al. Isochondodendrine and 2′-norcocsuline: Additional alkaloids from Triclisia

subcordata induce cytotoxicity and apoptosis in ovarian cancer cell lines. RSC Adv. 2017;7(70):44154–61.
44. Wang C, Cheng H, Wang S, Wei M, Du D. Plant community and the influence of plant taxonomic diversity on community stability and invasibility: A case study based on Solidago canadensis L. Vol. 768, Science of the Total Environment. 2021.
45. Wang XD, Li CY, Jiang MM, Li D, Wen P, Song X, et al. Induction of apoptosis in human leukemia cells through an intrinsic pathway by cathachunine, a unique alkaloid isolated from Catharanthus roseus. Phytomedicine. 2016;23(6):641–53.
46. Wu S, Yang L, Gao Y, Liu X, Liu F. Multi-channel counter-current chromatography for high-throughput fractionation of natural products for drug discovery. J Chromatogr A. 2008;1180(1–2):99–107.
47. Yarmukhamedova, N. F., Matkarimova, D. S., Bakieva, S. K., & Salomova, F. I. (2021). Features of the frequency of distribution of alleles and genotypes of polymorphisms of the gene Tnf-A (G-308a) in patients with rhinosinusitis and the assessment of their role in the development of this pathology. International Journal of Health & Medical Sciences, 4(1), 164-168. https://doi.org/10.31295/ijhms.v4n1.1671
48. Yu CC, Chen CA, Fu SL, Lin HY, Lee MS, Chiou WY, et al. Andrographolide enhances the anti-metastatic effect of radiation in Ras-transformed cells via suppression of ERK-mediated MMP-2 activity. PLoS One. 2018;13(10).
49. Zhang Y, Jia C, Zhang Y, Yang S, Dong Y, Wei D, et al. Chemical variability in volatile composition among five species of genus Solidago (Asteraceae). Biochem Syst Ecol. 2019;84:42–6.

Table 1. GC–MS oven temperature program

Rate	Temperature (°C)	Hold Time(min)
-	50.0	5.00
50.00	100.0	2.00
9.00	280.0	2.00

Table 2. List of phytochemical compounds identified in GC-MS from *Solidago Canadensis* and theirmolecular weight, molecular formula, and retention time

Compound	Name of compound	R T	Compound nature	Area	Area (%)	M W	M F
1	Bornyl acetate	9.915	Bornyl acetic acid	274652	0.15	196	$C_{12}H_20O_2$
2	Andrographolide	14.05	Green chiretta	654087	0.36	350	$C_{20}H_30O_5$
3	Z,Z,Z-1,4,6,9-Nonadecatetraene	14.37	Alkene compound	1165982	0.65	260	$C_{19}H_{32}$
4	trans-Chrysanthemal	14.51	Pyrethrins	441862	0.25	152	$C_{10}H_{16}O$
5	1-Oxaspiro[2.5]octane	14.74	Canonicalized	608489	0.34	206	$C_{14}H_{22}O$
6	Andrographolide	14.89	Lanhelian	1800858	1.00	350	$C_{20}H_{30}O_5$
7	4,7,10,13,16,19-Docosahexaenoic acid, methyl ester, (all-Z)-	15.07	Cervonic acid	1544565	0.86	342	$C_{23}H34O2$
8	11,11-Dimethyl-spiro [2,9]dodeca-3,7-dien	15.28	NF	820138	0.46	190	$C_{14}H_{22}$
9	Cyclohexanemethanol, 4-ethenyl-.alpha.,.alpha., Elemol	15.40	Elemol	1940317	1.08	222	$C_{15}H_{26}O$
10	Doconexent	15.46	Docosahexaenoic acid	2010669	1.12	328	$C_{22}H_{32}O_2$
11	Caryophyllene oxide	15.83	Epoxide	6155631	3.42	220	$C_{15}H_{24}O$
12	Cis-Lanceol	15.88	Canonicalized	4312296	2.40	220	$C_{15}H_{24}O$
13	1,3-Bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one	15.98	1,3-Bis-(2-cyclopropyl,2-methylcyclopropyl)-but-2-en-1-one	569066	0.32	258	$C_{18}H_{26}O$
14	Dactylol.	16.44	Dactylol	569265	0.32	222	$C_{15}H_{26}O$
15	β-Cembrenediol.	16.79	beta-Cembrenediol	1994925	1.11	306	$C_{20}H_{34}O_2$
16	Cyclopentaneacetaldehyde	16.91	Cyclopentaneacetaldehyde	2154785	1.20	166	$C_{10}H_{14}O_2$
17	Bicyclo[6.1.0]nonane	17.20	Bicyclononane	1345609	0.75	164	$C_{12}H_{20}$
18	8,11,14-Eicosatrienoic acid, methyl ester	17.39	Methyl ester methyl	649890	0.36	320	$C_{21}H_{36}O_2$
19	2H-Benzocyclohepten-2-one	17.49	2H-Benzocyclohepten-2-one.	2037891	1.13	180	$C_{12}H_{20}O$
20	1H-2,8a-Methanocyclopenta [a]cyclopropa[e]cyclodecen-11-one	17.66	1H-2,8a-Methanocyclopenta cyclopropa[e]cyclodecen-11-one	12325431	6.85	364	$C_{20}H_{28}O_6$
21	Cyclopropa[d]naphthalen-3-one, octahydro-2,4a,8,8-tetramethyl-, oxime	17.77	Cyclopropa[d]naphthalen-3-one, octahydro-2,4a,8,8-tetramethyl-, oxime	670228	0.37	235	$C_{15}H_{25}O$
22	Phthalic acid, isobutyl tridec-2-yn-1-yl ester	17.85	Phthalic acid	1489165	0.83	400	$C_{25}H_{36}O_4$
23	Aromadendrene oxide-(2)	18.06	Aromadendrene oxide 2	9068250	5.04	220	$C_{15}H_{24}O$
24	Kauran-18-al, 17-(acetyloxy)-, (4.beta.)-	18.25	18-Oxokauran-17-yl acetate	3884394	2.16	346	$C_{22}H_{34}O_3$
25	Dichloroacetic acid, tridec-2-ynyl ester	18.45	Dichloroacetic acid, tridec-2-ynyl ester	1865493	1.04	306	$C_{15}H_{24}C_{l2}O_2$
26	13,16-Octadecadiynoic acid, methyl ester	18.55	13,16-Octadecadienoic acid, methyl ester	3508478	1.95	290	$C_{19}H_{30}O_2$
27	Caryophyllene oxide	18.66	epoxide	1115666	0.62	220	$C_{15}H_{24}O$
28	1-Methyl-6-(3-methylbuta-1,3-dienyl)-7-oxabicyclo[4.1.0]heptane	18.85	NF	746465	0.41	178	$C_{12}H_{18}O$
29	Pentadecanoic acid	19.44	Pentadecanoic acid	9981610	5.55	242	$C_{15}H_{30}O_2$
30	7,10-Hexadecadienoic acid, methyl ester	20.32	Canonicalized	1075117	0.60	266	$C_{17}H_{30}O_2$
31	7-Hexadecenoic acid, methyl ester, (Z)-	20.40	Fatty acid methyl esters	2564769	1.43	322	$C_21H_{38}O_2$
32	Phytol	20.58	Florasol	18068403	10.04	296	$C_{20}H_{40}O$

33	Hexadecanoic acid, 15-methyl-, methyl ester	20.68	Methyl esters	413607	0.23	284	$C_{18}H_{36}O_2$
34	Cyclohexanol, 2-methylene-5-(1-methylethenyl)-	20.98	1-Methylethenyl	1301671	0.72	152	$C_{10}H_{16}O$
35	3-Tetradecyn-1-ol	21.26	3-Tetradecyn-1-ol	22814133	12.68	210	$C_{14}H_{26}O$
36	Octadecanoic acid, stearic acid	21.42	Stearic acid	1762591	0.98	284	$C_{18}H_{36}O_2$
37	(2Z)-3-pentyl-2,4-pentadien-1-ol	22.46	(2Z)-3-pentyl-2,4-pentadien-1-ol	1918292	1.07	312	$C_{20}H_{14}O_2$
38	2-Methyl-3-isopropenylcyclohexanol	22.61	-Methyl-3-isopropenylcyclohexanol	1309452	0.73	154	$C_{10}H_{18}O_2$
39	(2E,6E)-3,7-Dimethyl-2,6-nonadienyl acetate	22.78	3,7-Dimethyl-2,6-nonadien-1-ol acetate	7404451	4.12	210	$C_{13}H_{22}O_2$
40	Cyclobutanecarboxylic acid, tridec-2-ynyl ester	22.92	Cyclobutanecarboxylic acid	899714	0.50	278	$C_{18}H_{30}O_2$
41	1,6-Dibromo-2-cyclohexylpentane	23.18	Cyclohexene	15238700	8.47	310	$C_{11}H_{20}Br_2$
42	1,1-Propanedicarbonitrile, 1,2-dicyclohexyl-	23.39	Cyclohexane	7619186	4.23	258	$C_{17}H_{26}N_2$
43	(2E,6E)-3,7,11-Trimethyl-2,6-dodecadien-1-ol.	23.58	Sesquiterpenoids	2594439	1.44	224	$C_{15}H_{28}O$
44	2-Butenoic acid, 2-methyl-, dodecahydro-8-hydroxy-8a-methyl-3,5-bis(methylene)-2-oxonaphtho[2,3-b]furan-4-yl ester	23.97	2-Butenoic acid, 2-methyl-	634860	0.35	346	$C_{20}H_{26}O_5$
45	2,3,3-trimethyl-1,7-Octadiene	24.20	2,3,3-Trimethyl-1,7-Octadiene	937051	0.52	152	$C_{11}H_{20}$
46	3-Methyl-2-butenoic acid, dodec-9-ynyl ester	24.31	Methyl-branched fatty acids	874303	0.49	264	$C_{17}H_{28}O_2$
47	Methyl 12-oxo-9-dodecenoate	24.49	Methyl 12-oxo-9-dodecenoate	6064455	3.37	226	$C_{13}H_{22}O_3$
48	Butane-1,1-dicarbonitrile, 1-cyclohexyl-3-methyl	24.60	1-Cyclohexyl-3-methylpent-1-ene	1985208	1.10	204	$C_{13}H_{20}N_2$
49	Cyclohexane, (2-nitro-2-propenyl)-	24.82	Allyl hexahydrophenylhexanoate	3646507	2.03	169	$C_9H_{15}N_2$
50	Butane-1,1-dicarbonitrile, 1-cyclohexyl-3-methyl	25.06	1-Cyclohexyl-3-methylpent-1-ene	5103918	2.84	204	$C_{13}H_{20}N_2$
51	Cyclopentaneacetaldehyde	16.91	Cyclopentaneacetaldehyde	2154785	1.20	166	$C_{10}H_{14}O_2$

M.W=molecular weight; M.F=molecular formula; RT= retention time.

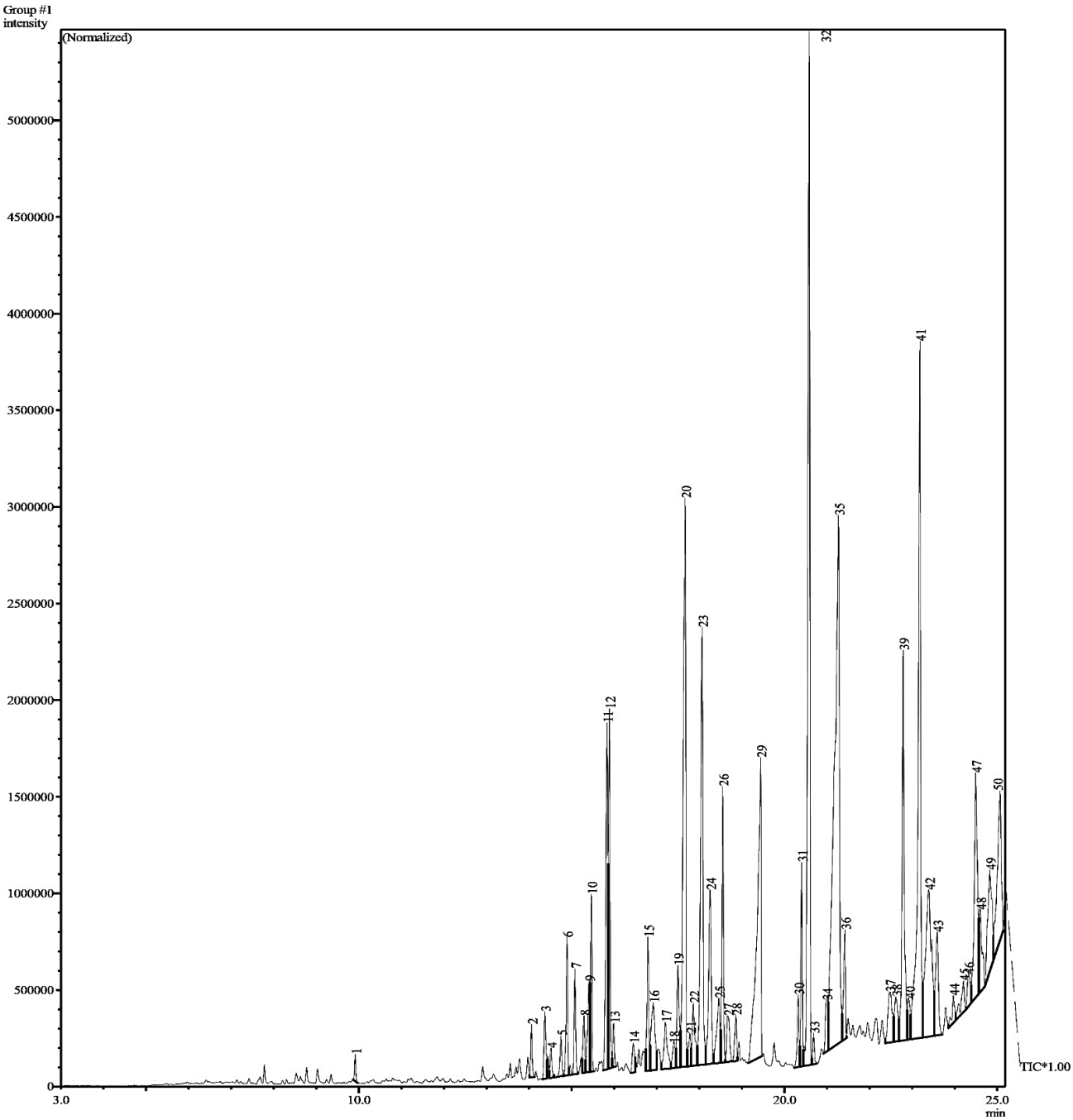


Fig. 1.GC–MS chromatography profile of *Solidago Canadensis* phytochemical compounds in hexane extract.

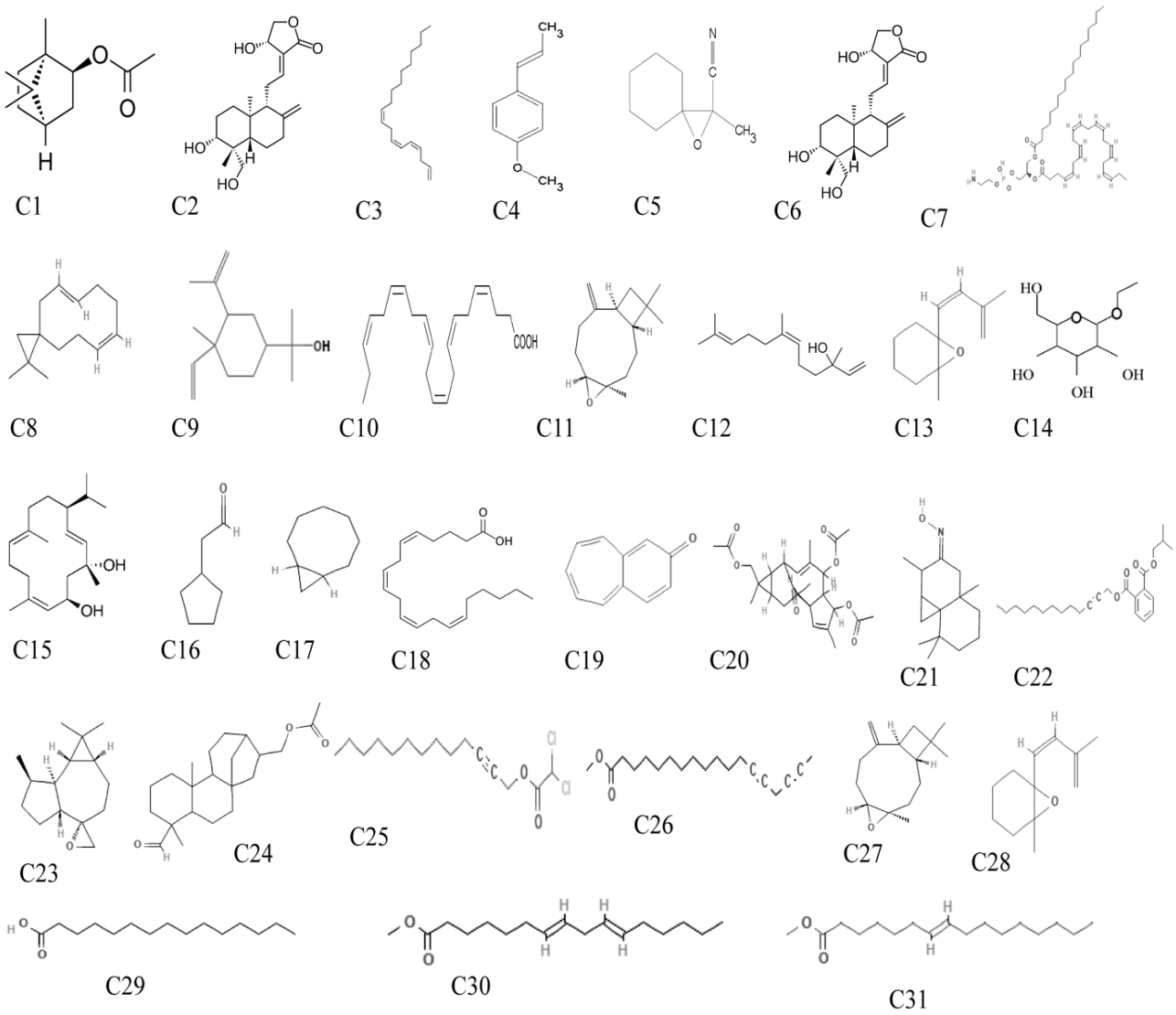


Fig. 2. Chemical structure of phytochemical compounds detected (1-31) of *Solidago Canadensis.*

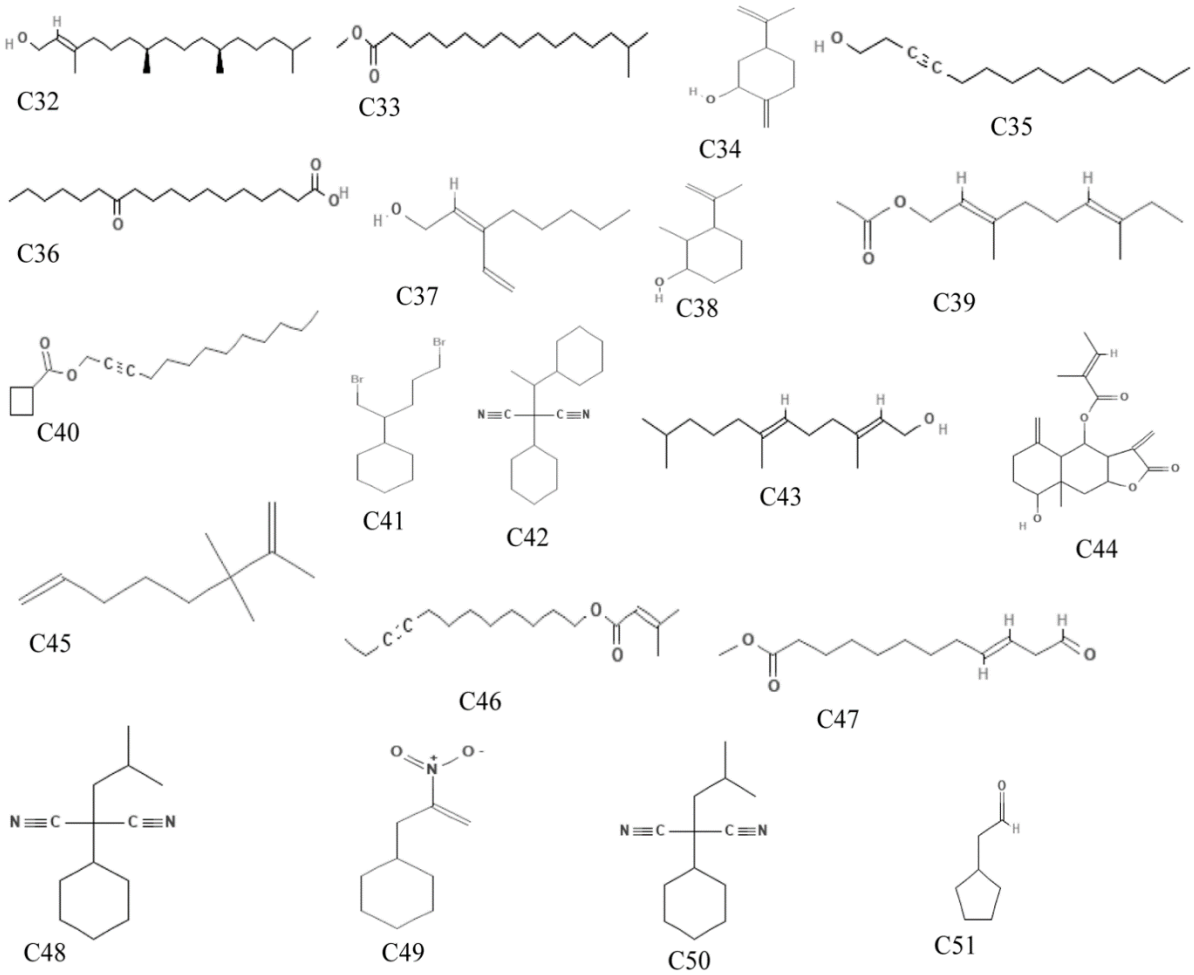


Fig. 3. Chemical structure of phytochemical compounds detected (32-51) of *Solidago Canadensis.*

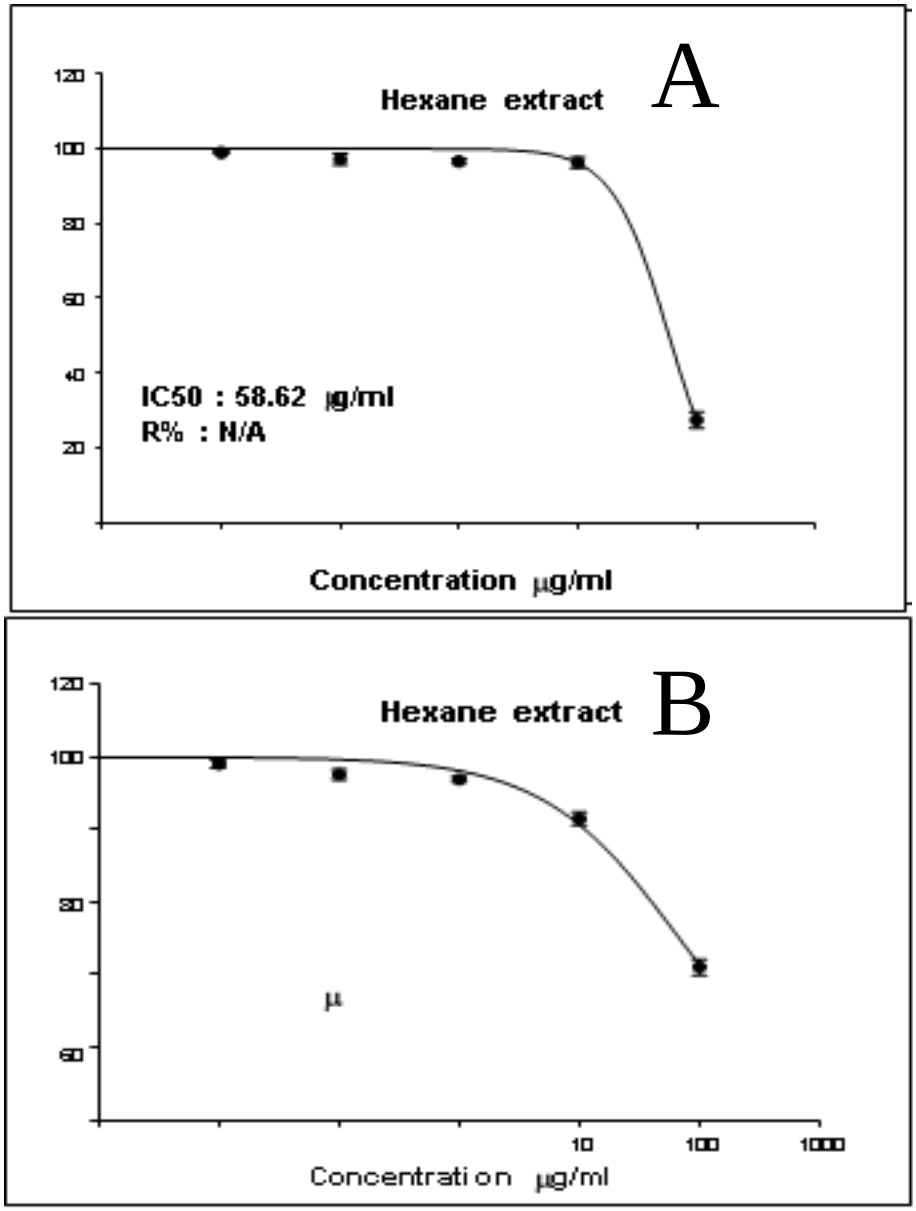


Fig. 4. (A) Evaluation of hexane extract on anti-colorectal adenocarcinoma. The concentration of the extracted phytochemicals was between 1 and 100 µg/mL. Exposition time: 48 h. Human tumor cell lines: colorectal adenocarcinoma (SW620) and type: WST-1 (Routine Analysis IC50) 5 concentration. (B) Anti-acute monocytic leukemia (AML). The concentration of the extracted phytochemicals was between 1 and 100µg/mL. Exposition time: 48 h. Human tumor cell lines: colorectal adenocarcinoma (SW620) and type: WST-1 (Routine Analysis IC50) 5 concentration.

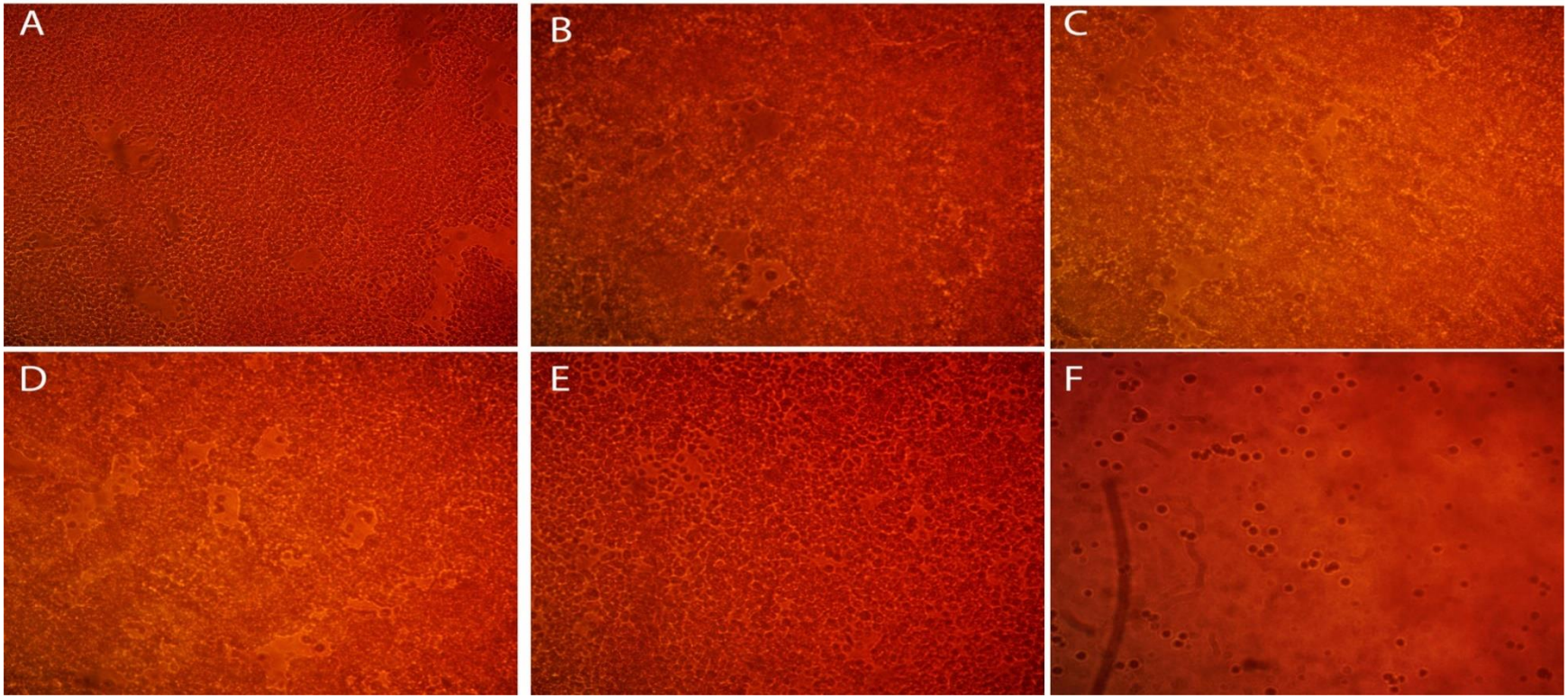


Fig. 5. The light microscopic surface of colorectal adenocarcinoma cell (×100 magnification). (A) A representative portion of a normal cell of colorectal adenocarcinoma (×100 magnification). (B) A representative portion of a cell of colorectal adenocarcinoma was treated with 0.01 µL/ml extracted phytochemicals. (C) A representative portion of a cell of colorectal adenocarcinoma was treated with 0.1 µL/ml extracted phytochemicals. (D) A representative portion of a cell of colorectal adenocarcinoma was treated with 1 µL/mL of extracted phytochemicals. (E) A representative portion of a cell of colorectal adenocarcinoma was treated with 10 µL/ml extracted phytochemicals. (F) A representative portion of a cell of colorectal adenocarcinoma was treated with 100 µL/mL of extracted phytochemicals.

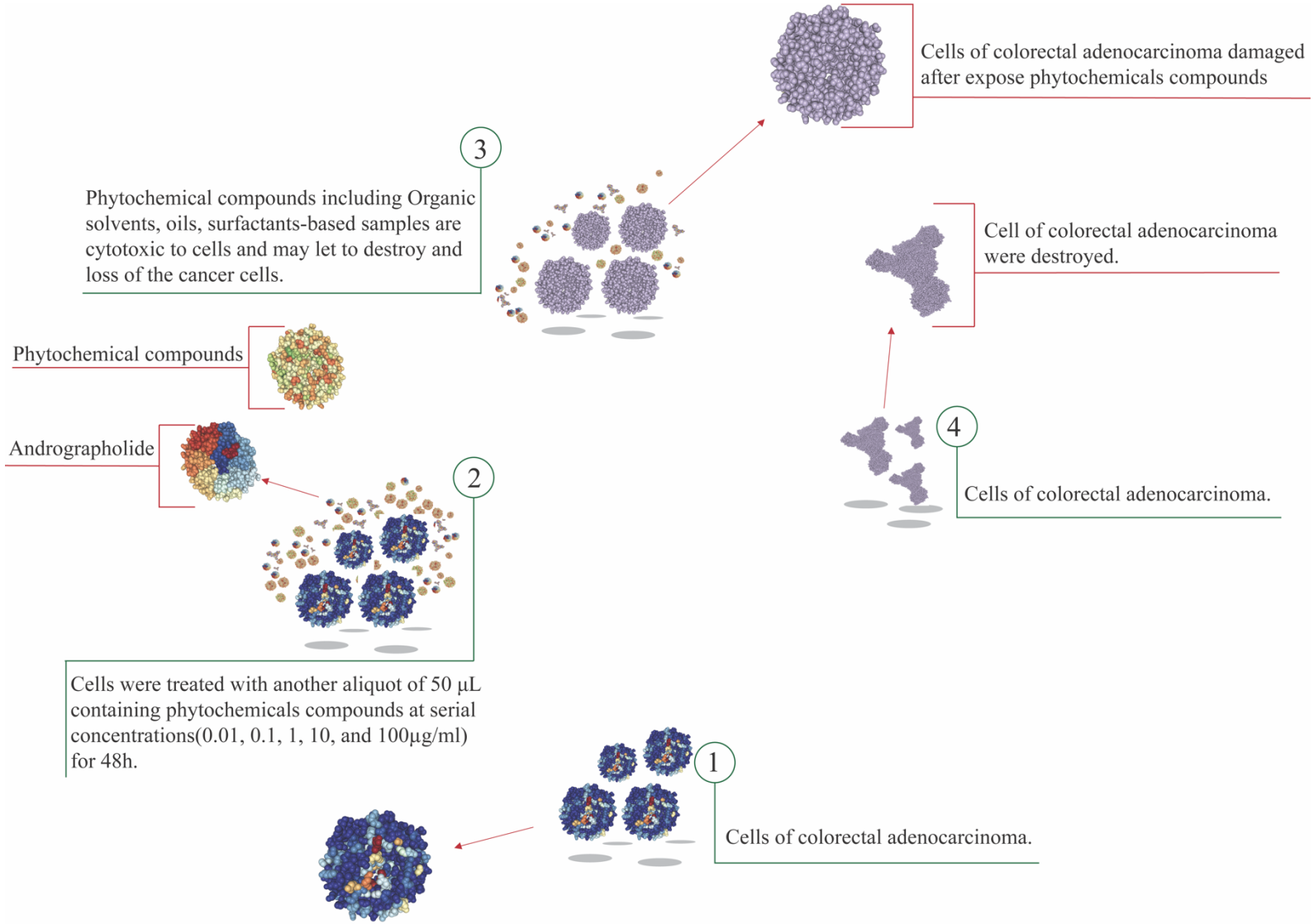
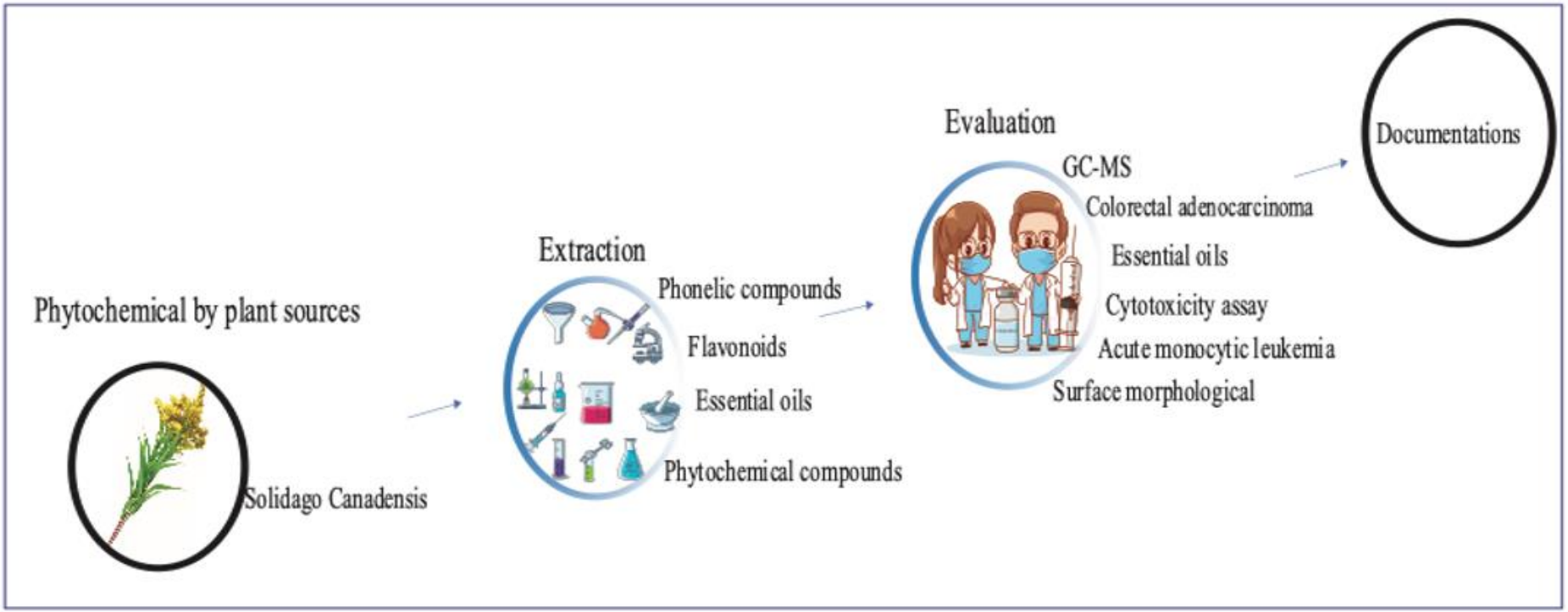


Fig. 6. Mechanisms of the effect of phytochemical components of *Solidago Canadensis*on colorectal adenocarcinoma byin-vivo testing.



Graphical abstract