International Journal of Innovative Research in Computer Science & Technology (IJIRCST)
ISSN: 2347-5552, Volume-10, Issue-2, Mar 2022
https://doi.org/10.55524/ijircst. 2022.10.3.83
Article ID CST1054, Pages 409-414
www.ijircst.org

An Overview on Anti-Chronic Myelogenous Leukaemia Efficacy of Spergulin-A

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ABSTRACT- One of the main causes of mortality in the 21st century has been cancer. Even among cancer, chronic myelogenous leukaemia (CML) is one of the main causes for cancer associated death. Despite its ubiquity the breadth of therapy is restricted by its high cost and lack of effectiveness. Spergulin –A, a saponin which is a triterpenoid, isolated from an n-butanol fraction of the flowering plant Glinus oppositifolius has been reported previously for its anti-leishmanial activity. In this study, Spergulin-A was isolated from Glinus oppositifolius and its Identification and structural confirmation was achieved by NMR, after which it was tested for its anti-CML action. As per the present results, Spergulin-A was found to cause growth inhibition and trigger apoptosis in K562, a cell line of chronic myelogenous leukaemia, origin. Moreover, Spergulin-A has demonstrated no detrimental effects against normal cell lines. Based on these results, it can be reasonably concluded that Spergulin-A may be used as an anti-CML agent.

KEYWORDS- Apoptosis, Chronic Myelogenous Leukaemia, Reactive Oxygen Species (ROS), Spergulin A.

I. INTRODUCTION

One of the lethal types of leukaemia is the Chronic Myeloid Leukaemia (CML) which caused by Philadelphia (Ph) chromosome i.e., reciprocal translocation, because of transfer of genetic matter between chromosome number 9 and chromosome number 22, yielding a gene, BCR-ABL1 classified as a fusion gene. This fusion gene interferes in various signalling pathways governing the cell cycle leading to uncontrolled cell division (Figure 1) [1][2]

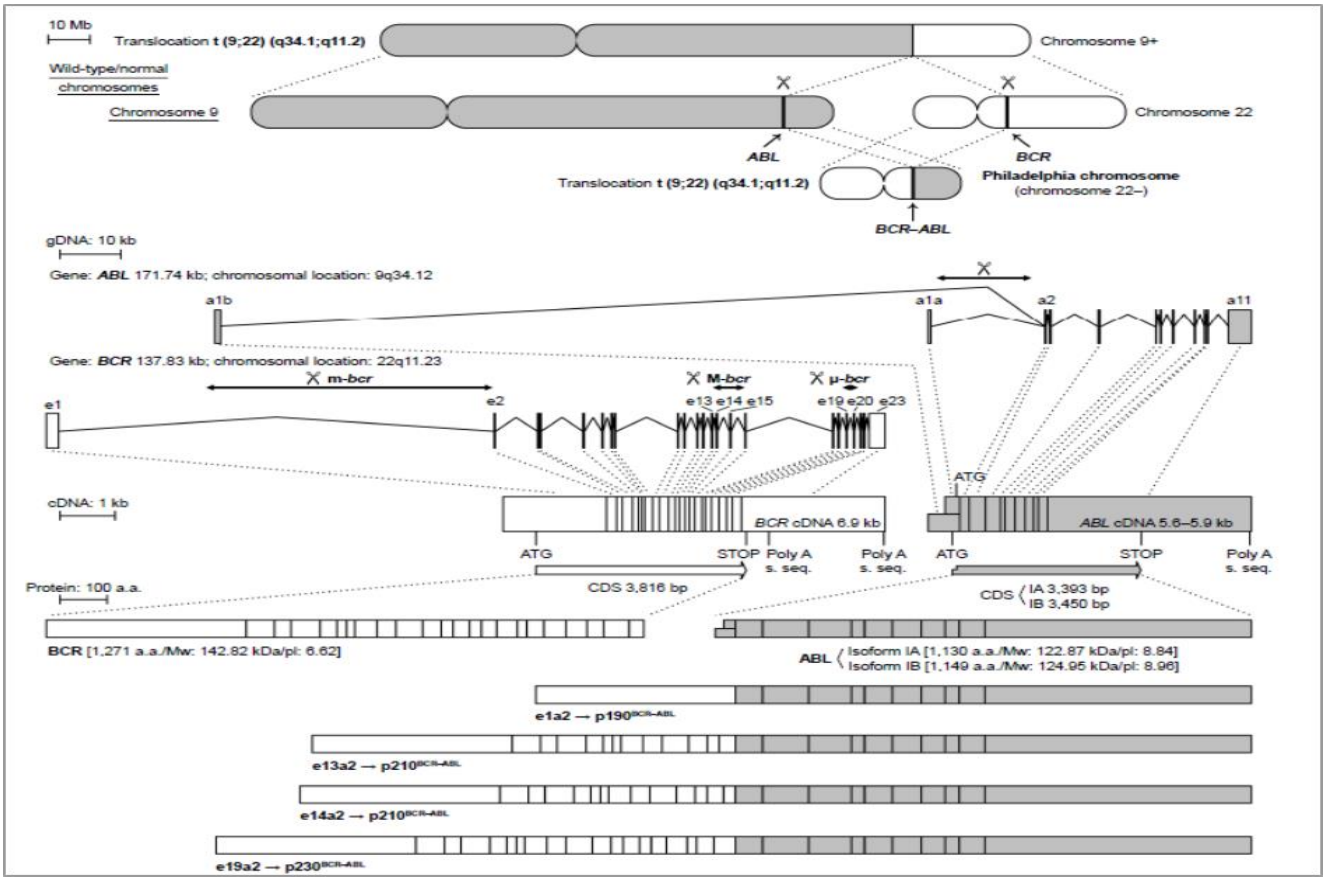

Figure 1: BCR–ABL, BCR genes being schematically represented with the proteins encoding the various gene combinations herewith

A. Inscription

Top panel: Position of the BCR and ABL loci on chromosomal number 22 and 9 correspondingly or the BCR ABL fusions gene loci on Philadelphia (Ph) chromosomes. Middle panel: the BCR (BCR1, HGNC, 1014) or ABL (formally ABL1; HGNC: 76) genes with their transcripts being depicted by their exon–intron architecture. Boxes indicated as a11 to a1a are for Exons for ABL with e23 to e1 to relating BCR genes, while bent lines denote introns [3–6]. The most recurring areas of interval points in the two genes are shown by left right arrows. The genes' proteins coding regions (CDS) have been listed below. Bottom panel: Both normal or fusion peptides encoded by crazy BCR but also ABL genomes, as well as the BCR ABL fusions genes, have been illustrated above for the appropriate manner. The p210 protein version is found in chronic myeloid leukaemia, with the p190 protein variant being linked with lymphoblastic leukemia and the p230 proteins variant associated Chronically Neutrophilic Leukaemia [7–11]. The JAK/STAT system controls numerous effectors by switching on STATs that are transcription factors with the ability to modulate cytokine receptors. The JAK/STAT pathway is involved in numerous processes for cell development through activation of transcription factors such as STATS. JAK2 phosphorylates and stabilizes the the BCR-ABL fusion protein at Y177 which has been further detailed in Figure 2 [4].

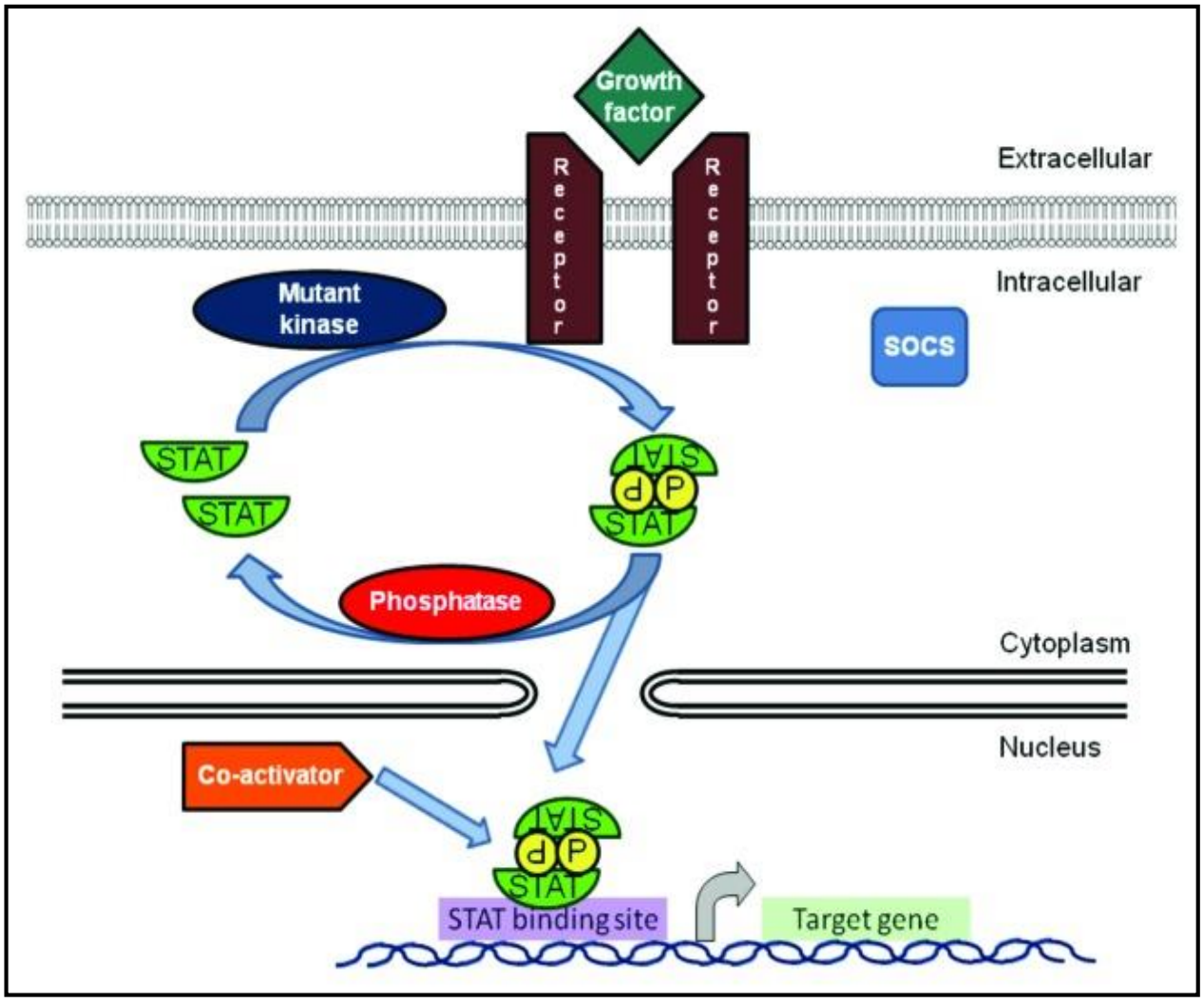

Figure 2: The JAK/STAT route regulates these effectors by “switching-on” STATs that are transcription factors

Transcription factors, namely STAT3 and STAT5, are up-regulated in CML through different mechanisms and decreased activity of negative regulators such as phosphatases and SOCS protein(12). The Ras/MAPK/ERK pathway plays an important role in cell growth and differentiation. In Ph chromosome positive CML cells, the fusion protein “switches on” the RAS/RAF/MEK/ERK route, resulting in the uncontrolled proliferation of CML cells which has been further elaborated in Figure 3 [13].

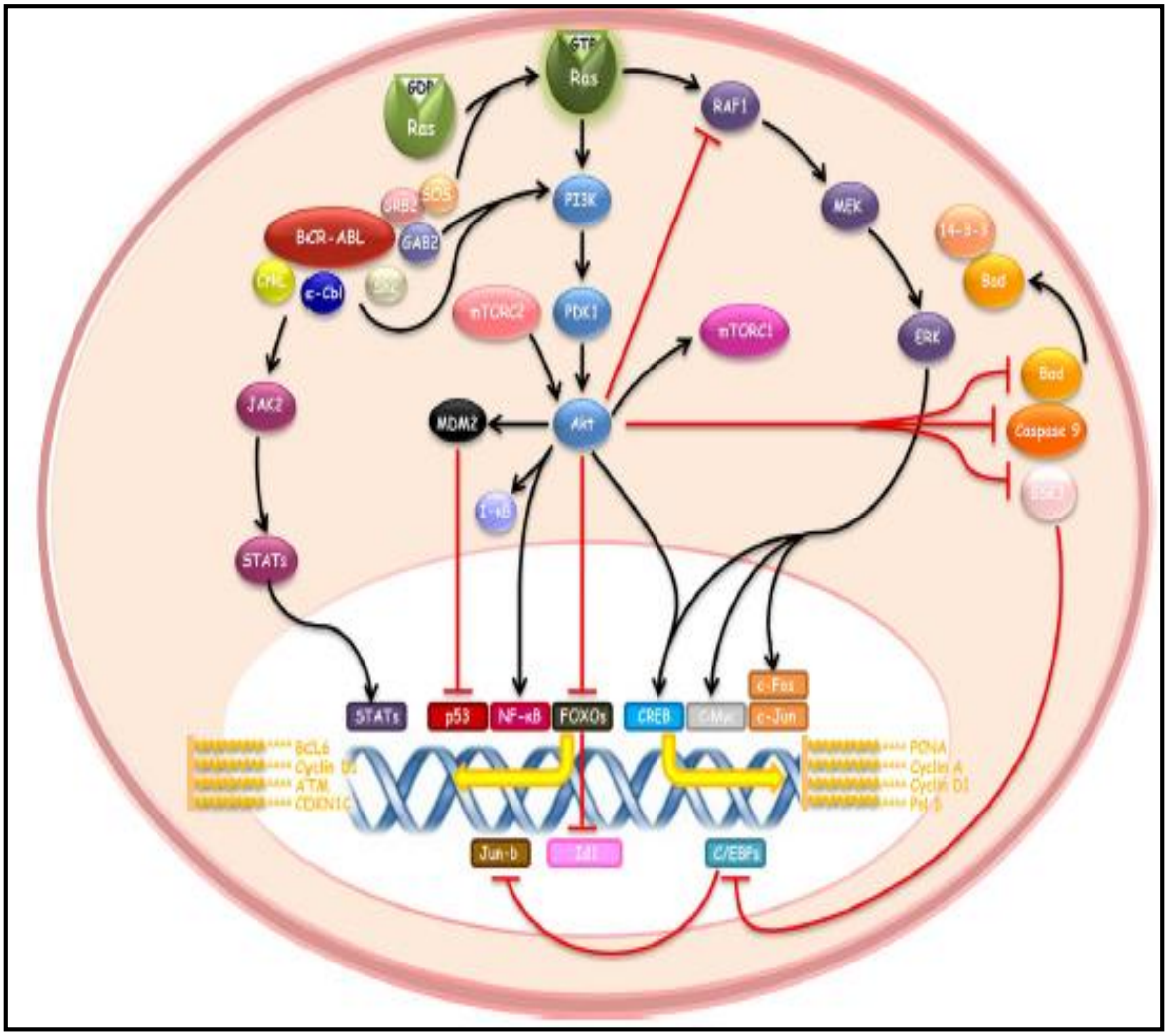

Figure 3: Signalling pathways that are activated in chronic myeloid leukaemia

Leukaemia Stem Cell (LSC) transition from a normal tissue is a multileg process which involves numerous genetic alterations, which leads in abnormal cellular processes which normally regulate cell proliferation and differentiation[(14–17]. Furthermore, basic "switching on" of the MEK/RAF/ERK, PI3K/AKT or JAK/STAT signalling pathway are extremely significant causes for the metamorphosis of LSCs. Abbreviations are as follows: As a Son of Sevenless, I'm on a mission. GRB2 stands for Growth factors receptors obligated proteins 2, GAB2 stands for GRB2-associated binding proteins 2, MEK stands for Mitogen activated kinase activity, PI3K stands for Phosphatidylinositol 3-kinase, ERK stands for Extracellular signal-regulated kinase, PDK1 stands for Phosphoinositide dependent kinase-1, mTORC stands for Mammalian MDM2 is a homolog of Mouse Double Minute 2 (MDM2). NF-B stands for Nuclear factor kappa B, I-B stands for Inhibitor kappa B, FOXO stands for Forkhead box O, and CREB stands for cAMP response elements binding protease, C/EBP stands for CCAAT/enhancer protein complex, Id1 stands for Inhibitor of differentiation 1, JAK stands for Janus kinase, STAT stands for Signal transcription factors, BCL6 stands for B-cell lymphoma 6, CDKN1C stands for Cyclin-dependent kinase (CDK)-inhibitor 1C, ATM stands for Ataxia Telangiectasia Modified, pol stands for DNA polymerase [5].

Characterization and Identification and of Spergulin-A

As per the earlier reports, Spergulin A was isolated from the n-butanolic fraction. Thereby the n-butanolic fraction was purified by the use of column chromatography; regarding which an amorphous white compound was gained. Molecular formula C35H58O11S (Figure 4) and its corresponding NMR data was similar to as reported earlier[18].

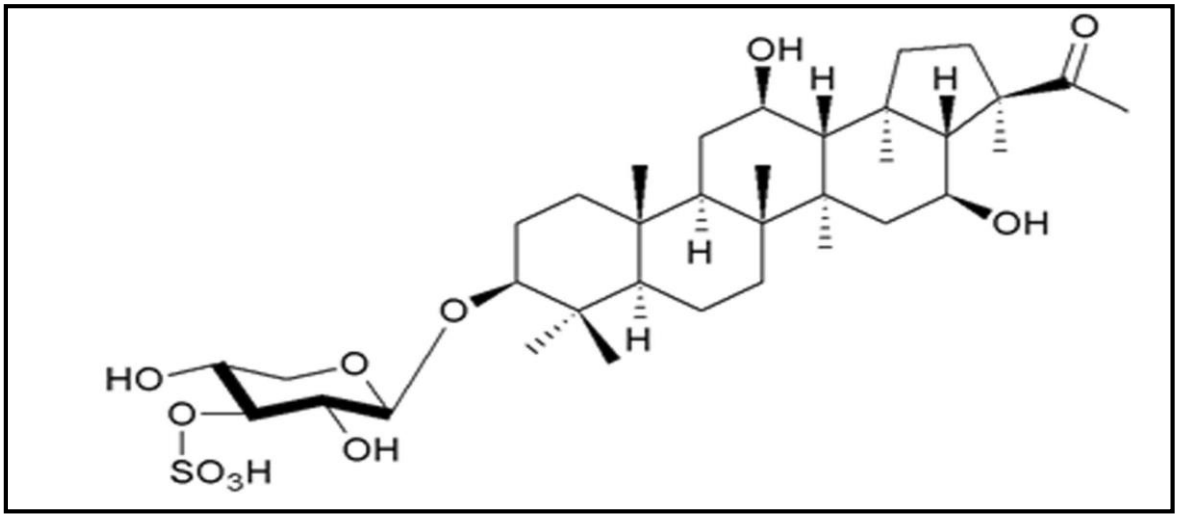

Figure 4: Structure and NMR data of Spergulin A

The ariel parts of the flowering plant Glinus oppositifolius (Family Molluginaceae) has been reported to have numerous biological activities like its role in treatment of gastric disorders and malaria. There are reports of its anticancer role as well [19]. Some triterpenoid saponins like Spergulacins A, Spergulacin, Spergulin A, Spergulins-B and 3-O-(β-D-xylopyranosyl)-spergulagenins-A have been isolated earlier. Among the tripenoid saponins, Spergulin A has been reported for its anti-Leishmanial activity. In this paper, the anti- Chronic myeloid leukemia activity of Spergulin A has been elucidated[20].

Preparation of methanolic fractions of G. oppositifolius

Firstly, G. oppositifolius's aerial parts were dried in shade (2 kg) and which were then degreased at room temperatures for the 72 h by petroleum ether (65–85°C, 4.5 L × 4). The marc was extracted with 4.5 L of methanol at air temp for 48 hours, after which the extraction was filtered as well as the methanol then dehydrated or recrystallized under lower pressure to obtain the crude methanol extract (12 g). A fraction of the MeOH extract (ME) was dissolved in milli-Q water but also separated into EtOAc or butanol in that orderThe aqueous fraction (AF; 3.3 g), EtOAc fraction (EAF; 4.6 g), and n-BuOH fraction (NBF; 5.1 g) were all lyophilized and evaporated under vacuum to obtain the AF, EAF, and NBF, which have all been retained at 4°C for subsequent use [21].

Amongst these portions, butanol had shown promising leishmanial killing activity. About 5 g of this portion was submitted to the columns chromatography by Diaion HP 30 (200 g) or was rinsed with the water surveyed by 40%, 50%, 70%, 90%, or 100% of methanol to obtains a total of the six portions. Portions eluted with 51percent MeOH showed nearly comparable spot on TLC or yielded 10 mg of Spergulin-A in a process as reported earlier [22][23].

Growth inhibitory effect of Spergulin-A on K562 cells

To assess the potency of the Spergulin-A against Chronic myeloid leukaemia (CML), Spergulin-A was evaluated for its growth inhibitory effect on K562 cell lines utilizing the MTT assay. After 24 h treatment, it was found that Spergulin A showed a concentration dependent growth inhibition in K562 cell lines, with an IC50 values of 48.24 µg/ml (Figure 5) without any growth inhibitory activity on the Normal human embryonic kidney 293 (nHEK-293) cell lines (data not shown). This implies that Spergulin A unlike on CML cells has no growth inhibitory activity on normal cells[24].

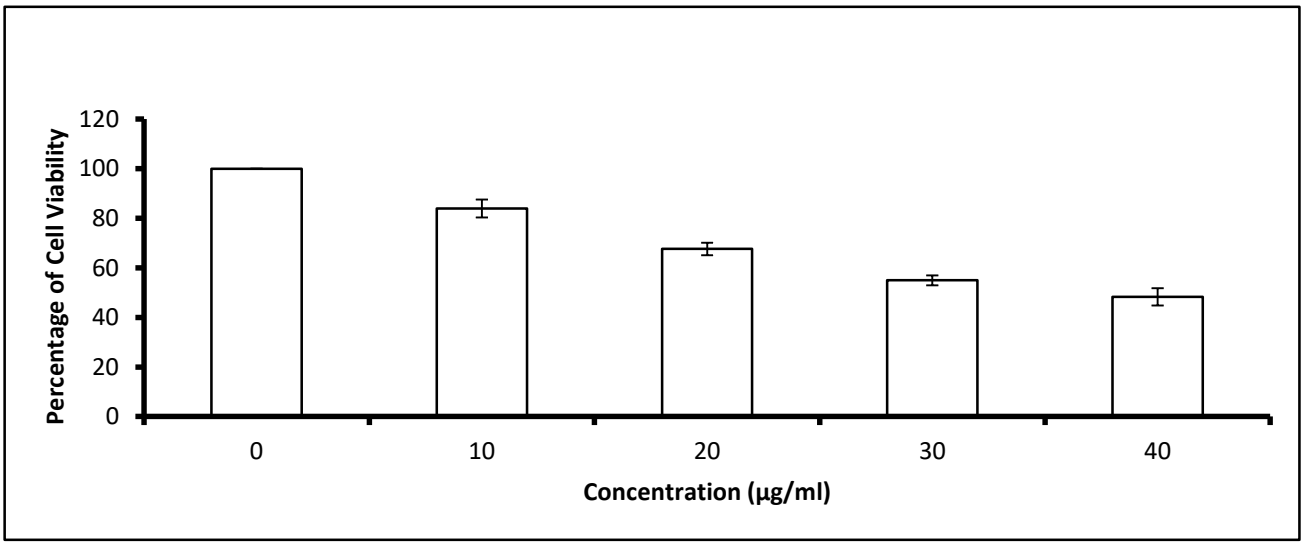

Figure 5: Graph showing growth inhibitory efficacy of Spergulin A

The CML cells; K562 showed a dose dependent decrease in the percentage of viable cells after 24 h[25]. The values were statistically significant with respect to the control or un-treated cells with $P<0.05$.

II. DISCUSSION

In RPMI supplemented with Foetal bovine serum but also antibiotics, the CML cell line K562 or regular humans embryonic kidney human embryonic nHEK were cultured. Both the cell lines were exposed with Spergulin A at a concentration of 0, 10, 20, 30, 40 and 50 µg/ml for 24 and the percentage percentage inhibition was measured by MTT test. After 24 h, there was a dosage dependent reduction in the viability of the K562 cells with an IC50 value of 48.24 µg/ml. However there was no significant reduction in the viability of nHEK cells suggesting that Spergulin A may be further investigated for its anti-CML function. Most of the anti-cancer medicines are renowned for their expensive price which primarily arises owing to the absence of effective producing sources. As G. oppositifolius is a reasonably widespread blooming plant, thus commercial quantity of Spergulin-A may be readily generated.

III. CONCLUSION

Chronic myeloid leukaemia (CML) is one of the main cause of death among leukaemia patients whose treatment is hampered by high cost and toxicity. This study has tried to discover a lead chemical against CML. Literature study on anti-cancer property of medicinal plants have shown the biological activity including its anti-cancer activity of a flowering plant Glinus oppositifolius. Furthermore, as per previous studies a triterpenoid saponin known as Spergulin-A has demonstrated anti-leishmanial action. Thereby, Spergulin-A was selected for investigation of its anti-CML efficacy. Firstly, ariel portions of G. oppositifolius were dried in the shade and their fat content was reduced by petroleum ether. Following this, the plant material underwent extraction by methanol. The extract was then filtered and lyophilized. The lyophilized powder was then dissolved in butanol and was then lyophilized again. For future usage, the lyophilized powder was deposited in an airtight container but also kept at 40°C. Then, roughly 5 g of this component was submitted to column chromatography on a Diaion HP 30 (200 g) column as well as washed with water before being split into six pieces with 40%, 50%, 70%, 90%, or 100% methanol. On TLC, samples eluted with 50% MeOH showed almost similar spots or generated 10 mg of Spergulin-A.

REFERENCES

[1] Soverini S, De Benedittis C, Mancini M, Martinelli G. Best Practices in Chronic Myeloid Leukemia Monitoring and Management. Oncologist. 2016;

[2] Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016.

[3] Sharma K, Goswami L. RFID based Smart Railway Pantograph Control in a Different Phase of Power Line. In: Proceedings of the 2nd International Conference on Inventive Research in Computing Applications, ICIRCA 2020. 2020.

[4] Sharma S, Hussain MS, Agarwal NB, Bhurani D, Khan MA, Ahmad Ansari MA. Efficacy of sirolimus for treatment of autoimmune lymphoproliferative syndrome: a systematic review of open label clinical studies. Expert Opinion on Orphan Drugs. 2021.

[5] Swarup N, Chowdhary Z, Nayak MT, Shami S. Jaw Swelling Back with Vengeance. Indian J Otolaryngol Head Neck Surg. 2020;

[6] Jain V, Garg R. Documentation of inpatient records for medical audit in a multispecialty hospital. Pravara Med Rev. 2019;

[7] Sinha P, Rastogi R, Pratap V, Singh VK. Role of carotid doppler and coronary CT angiography as predictors of coronary artery disease in patients of acute stroke. J Int Med Sci Acad. 2018;

[8] Kaur S, Muninarayanappa N V. A study to assess the effectiveness of awareness programme in term of knowledge regarding early symptoms of myocardial infarction among bank employees of selected banks at Moradabad, U.P. Indian J Public Heal Res Dev. 2017;

[9] Rastogi R, Budhiraja V, Jain SK, Sharma N, Garg R, Nafees H. Morphological pattern of Crista terminalis, Musculi pectinati and Taenia sagittalis with applied significance. J Morphol Sci. 2016;

[10] Chopra A, Rao NC, Gupta N, Vashisth S, Lakhanpal M. The predisposing factors between dental caries and deviations from normal weight. N Am J Med Sci. 2015;

[11] Verma P, Gupta Verma D, Khosa R, Kumar S, Basavaraju S, Patwardhan N. Combined use of frontal sinus and nasal septum patterns as an aid in forensics: A digital radiographic study. N Am J Med Sci. 2015;

[12] Bar-Natan M, Nelson EA, Xiang M, Frank DA. STAT signaling in the pathogenesis and treatment of myeloid malignancies. JAK-STAT. 2012;

[13] Bertacchini J, Ketabchi N, Mediani L, Capitani S, Marmiroli S, Saki N. Inhibition of Ras-mediated signaling pathways in CML stem cells. Cellular Oncology. 2015.

[14] Devi P, Bhavle R, Aggarwal A, Walia C. Esthesioneuroblastoma presenting as tooth pain. J Oral Maxillofac Pathol. 2014;

[15] Rallan M, Rallan NS, Goswami M, Rawat K. Surgical management of multiple supernumerary teeth and an impacted maxillary permanent central incisor. BMJ Case Rep. 2013;

[16] Ravindra S V., Srinivasa Raju M, Sunitha JD, Taneja N, Chandra S, Mahajan S, et al. Intraoral Superficial Angiomyxoma of the Upper Alveolus: Report of a Unique Case. Case Rep Med. 2012;

[17] Jagtap MT, Tripathi RC, Jawalkar DK. Depth accuracy determination in 3-d stereoscopic image retargeting using DMA. In: Proceedings of the 2020 9th International Conference on System Modeling and Advancement in Research Trends, SMART 2020. 2020.

[18] Kumar D, Shah V, Ghosh R, Pal BC. A new triterpenoid saponin from Glinus oppositifolius with α-glucosidase inhibitory activity. Nat Prod Res. 2013;

[19] Chakraborty T, Paul S. Glinus oppositifolius (L.) Aug. DC.: A Repository of Medicinal Potentiality. Int J Phytomedicine. 2017;

[20] Brognara E, Lampronti I, Breveglieri G, Accetta A, Corradini R, Manicardi A, et al. C(5) modified uracil derivatives showing antiproliferative and erythroid differentiation inducing activities on human chronic myelogenous leukemia K562 cells. Eur J Pharmacol. 2011;672(1–3):30–7.

[21] Greaves MF. Analysis of the Clinical and Biological Significance of Lymphoid Phenotypes in Acute Leukemia1. 1981;41(November):4752–66.

[22] Gupta RK, Kumar D, Chaudhary AK, Maithani M, Singh R. Antidiabetic activity of Passiflora incarnata Linn. in

streptozotocin- induced diabetes in mice. J Ethnopharmacol. 2012;
[23] Verma KG, Kumar Kaushik B, Singh R. Monte Carlo Analysis of Propagation Delay Deviation due to Process Induced Line Parasitic Variations in Global VLSI Interconnects. Int J Comput Appl. 2011;
[24] Myasnikov AG, Kundhavai Natchiar S, Nebout M, Hazemann I, Imbert V, Khatter H, et al. Structure-function insights reveal the human ribosome as a cancer target for antibiotics. Nat Commun. 2016;7:1–8.
[25] Li Y, Zou D, Zhao Y, Mi Y, Wang J, Qiu L. Clinical characteristics and outcomes of adults with philadelphia chromosome positive and/or bcr-abl positive acute lymphoblastic leukemia: A single center study from China. Leuk Lymphoma. 2010;51(3):488–96.