Effects of micro-colloidal Rhodomyrtus tomentosa on MMP9, GLUT-1, and IL-1β expression in Rattus norvegicus cervical cancer

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Abstract

Context: Rhodomyrtus tomentosa has the potential to contain compounds that enhance health. One type of disease that requires antioxidants in its healing is cancer. R. tomentosa extract was resized to nano size to optimize cell permeability.

Aims: To analyze the effects of micro-colloidal leaves extract of R. tomentosa (MR) on MMP9, GLUT-1, and IL-1β expression in cervical cancer.

Methods: Wistar rats were divided into five treatments, namely untreated (C-), cervical cancer (C+), and a cervical cancer rat model that was given R. tomentosa extract (MR) 100 mg/kg (MR100), 200 mg/kg (MR200), and 400 mg/kg (MR400). After receiving the extract for 30 days, all groups were analyzed using an immunohistochemical technique to detect MMP9, GLUT-1, and IL-1β antibodies.

Results: From the statistical analysis, there was a substantial difference in the expression of MMP9, GLUT-1, and IL-1 in the C+ group compared to the C-, MR100, MR200, and MR400 groups (p<0.005; p<0.002; p<0.001 p<0.01, respectively). Unrestrained cell development, asymmetric cell shape, a sizeable nucleus-to-cytoplasm ratio, and various nucleus-form variants, and when MR was administered, the cervical histology of the tissues began to improve, similar to group C. In this group decreases the distance between the tumors, slows the growth of the carcinoma, and permits the nucleus to form appropriately in a cervical cancer cell was observed. Dosages of 200 and 400 mg/kg improved the histology of cervical tissue while decreasing MMP-9, GLUT-1, and IL-1β expression.

Conclusions: Rhodomyrtus tomentosa ethanolic extract show antimetastatic properties and could be analyzed as an anticancer therapy in the future.

Keywords: GLUT-1; IL-1β; MMP9; myrto; plant extracts; uterine cervical neoplasms.
INTRODUCTION

Cancer is still Indonesia’s most dangerous and deadly, especially cervical cancer. According to GLOBOCAN data, the incidence of new cases of cervical cancer in women ranges from 32,469 cases (17.2%) to 18,279 (8.8%) (Aoki et al., 2020). Low molecular weight protein is a crucial biomarker in the diagnosis of cancer at an early stage (Zafar et al., 2020). Because surface coating helps molecular, cellular, and biological roles in cell signaling (Hasan et al., 2021). In addition to low molecular weight proteins, biochemical and metabolic profiles also help to diagnose cancer early detection (Manzoor et al., 2022). The HPV virus, specifically the papillomavirus, causes nearly 95% of cervical cancer in women (human papillomavirus). Medical infections such as human papillomavirus infection (HPV) can progress to dysplasia or complete recovery and usually occur in women of reproductive age (Spagnoletti et al., 1999).

Matrix metalloproteinases 9 (MMP9) is one of the most complex types of MMP proteins because it can degrade extracellular matrix (ECM) components and is involved in pathophysiological functions (Mondal et al., 2020). MMP-9 overexpression and dysregulation have been linked to various diseases, including cancer (Mondal et al., 2020). Therefore, MMP-9 inhibition is an essential therapeutic approach in treating various diseases, including cancer, to repair cells in an organ. In addition, MMP-9 inhibitors can be anti-cancer agents (Mondal et al., 2019). Blocking MMP9 activity using an MMP9 antibody in the active form of gelatinase could inhibit metastasis in the MMTV-PyMT model (Omyong et al., 2019).

Glucose transporter-1 (GLUT-1) is essential for treating cancer in most normal tissues. However, it is occasionally not seen in benign epithelial tumors or healthy epithelial tissue. Indicators of vascular and metabolic needs, such as GLUT-1 expression in cancer, have therapeutic consequences for survival during treatment (Carvalho et al., 2011). Malignant cells frequently have higher glucose metabolic values than normal cells to support cell growth (Pragallapati and Manyam, 2019; Zambrano et al., 2019).

The immune system components that surround cancer cells and can be used to prevent cancer are lymphocytes, NK cells, macrophages, and cytotoxic T lymphocytes (Bald et al., 2020). Once these four cells identify cancer as foreign cells, they will exterminate them. The body produces IL-1β but it can also be made artificially in a laboratory. Interleukin-1 beta (IL-1β) is expressed by various cells, including macrophages, NK cells, monocytes, and neutrophils (Yang et al., 2020). Estrogen levels can suppress cytokine production, but hormonal influence also increases cytokine expression. Estrogen can stimulate the production of IL-1β, promoting tumor activity (Yu et al., 2019). The addition of cytokines can increase the expression of adhesion molecules, tissue factors, and mannosylation proteins in the cell (Yang et al., 2020). TNF-alpha antibodies or soluble TNF-alpha receptors partially inhibit IL-1β induced proliferation (Yang et al., 2020). IL-1β promotes the proliferation of carcinoma cells and can also increase the activity of the enzyme aromatase, which causes cells to produce more estrogen (Zhang et al., 2020).

Rhodomyrtus tomentosa (Aiton) Hassk. It is a Myrtaceae ethnomedicinal plant. Another name for this plant is harmonizing. In Southeast Asia, including Indonesia, this plant has traditionally been used to treat inflammatory and infectious conditions such as colitis, diarrhea, dysentery, abscesses, and bleeding (Vo and Ngo, 2019). Additional pharmacological studies with this plant have suggested that the extract can be used for antibacterial and hepatoprotective properties (Zhang et al., 2018). Rhodomyrtone is this plant's bioactive acyl phloroglucinol molecule (Vo and Ngo, 2019). This plant has been shown to repair lung tissue damaged by smoking (Ilyas et al., 2019), decrease lipid peroxidation activity by increasing HSP-70 expression in hypertension (Ilyas et al., 2019), repair testicular tissue, placenta, and burns due to diabetes (Ilyas and Situmorang, 2018; Irianti et al., 2020; Manurung et al., 2021). In addition, R. tomentosa has high antioxidants, and its phenolic content can be a potential source of health-supporting substances (Vo and Ngo, 2019).

Medicinal effects of this plant also can be attributed to the many phytoconstituents contained in it, especially the rhodomyrtials A and B. Rhodomyrtone, rhodomyrtials A and B inhibited A431 cell metastasis by reducing MMP-2/9 activities (Tayeh et al., 2017). Furthermore, derivates related to acyl phloroglucinol, such as myrtucommuacetalone, myrtucommulone A, and semimyrtucommulone, from R. tomentosa may prevent or delay the progression of inflammation by reducing the level of IL-1β (Srisuwan et al., 2018) and increasing the level of GLUT-2 in the diabetic wound case (Dwita et al., 2021). Therefore, the anticancer activity possessed by this plant is exciting to discuss with a higher level of validity, which is tested in a laboratory by directly observing the expression of proteins that affect cancer growth, such as MMP-2/9, IL-1β, and GLUT-1. In previous studies, this plant has been investigated for its anticancer properties in cervical cancer cases by assessing its TGFβ1 and VEGFR expression (Situmorang et al., 2023). That study sup-
ports that R. tomentosa suppresses the amount of expression of this pro-cancer protein in the tissues tested. That discovery will be further strengthened by assessing several proteins that influence other cancer growth processes, such as MMP-2/9, IL-1β, and GLUT-1, to perfect the anticancer character of R. tomentosa, especially in the cervical cancer case because cervical cancer placed in the second rate of female cancer case in this world based on the data of Global Cancer Observatory (2020).

MATERIAL AND METHODS

Materials

Rabbit polyclonal GLUT1 IHC antibody was used as an antibody (Catalog Number: IW-PA1120, Company: IHC WORLD, Ellicott City, USA). EPR22140-154 - BSA and IL-1β polyclonal antibody, storage buffer: PBS with 50% glycerol, 1% BSA (Catalog BS-0812R), rabbit polyclonal MMP9 antibody (ab237782).

Preparation of micro-colloidal R. tomentosa (MR)

R. tomentosa leaves were collected from Humbahas Regency’s Lintong Nihuata Sub-district, Indonesia (02°4’20” North latitude and 98°56’20” East longitude). The voucher was identified and authenticated by Dr. Etti Sartina Siregar, M.Si, and deposited into the Medanense Botanical Herbarium (Registration number: 298/MEDA/2022) at Universitas Sumatera Utara, Medan, Indonesia.

R. tomentosa leaves and twigs were separated, cleaned of any dirt or dust attached, and smoothed after drying for seven days at room temperature. Next, 500 g of dry R. tomentosa flour was thoroughly mixed in 96% technical ethanol for 24 h at room temperature. Maceration with a 96% specialized absolute ethanol yielded an ethanolic extract of R. tomentosa. First, the emulsification products were filtered through a Buchner funnel and a vacuum pump. The purified residue was then taken and dissolved multiple times extra by the same procedure. Next, the concentrated ethanolic extracts were dehydrated for eight hours after being concentrated in a rotary vacuum evaporator to generate a solid ethanol extract.

To make the micro-colloidal R. tomentosa (MR), the leaves of R. tomentosa were sonicated to produce the following ethanol extract: 0.5 milligrams of R. tomentosa extract were added to a Tween 20 solution. The mixture was homogenized after the addition of carpool 90. After adding PEG-400, the mixture was sonicated. Finally, the prepared product was diluted in filtered water (1:100) and homogenized with an ultrasonic instrument (Vevor Ultrasonic Cleaner JPS-20A, 2211-0046, Ulangge, China) to create micro-colloidal R. tomentosa (MR) (Sonicator Ultrasonic Homogenizers and Emulsifiers).

Experimental animals

Thirty female albino rats of the Wistar strain weighing 120-180 g were housed in neat, well-ventilated propylene cages and kept under standard laboratory conditions (light/dark cycle 12 h, 24°C). The animals were obtained from the Faculty of Mathematics and Natural Science, University of North Sumatra. They were allowed to adjust for two weeks before the experiment began. They were fed as milled corn or pellets and given drinking water ad libitum. Rats were divided into five groups, with six animals in each treatment group. Six rats as negative control (C-) and twenty-five with cervical cancer were injected with benzopyrene dissolved in maize oil once at 50 mg/kg BW. Those twenty-five cervical cancer rats were used as the treatment group and divided into the positive control (C+), MR100 (by giving 100 mg BW of MR), MR200 (by giving 200 mg BW of MR), and MR400 (by giving 400 mg BW of MR). The rats showed symptoms of cancer after three months of injection and already visible lumps around the vagina, which are suspected to be tumors (Simanullang et al., 2022; Viswanathan et al., 2019). After getting the positive tumor, MR administration was held for 30 days and dissected. Then, rats were dissected to extract the cervix after they had been sedated with 300 mg/kg BW ketamine and 15-30 mg/kg BW xylazine (Simanullang et al., 2022). All experiments and protocols described in the present study were approved by the Animal Research Ethics Committees/AREC with an approval number 0304/KEPH FMIPA/2022. The experimental procedures and animal care was performed by the “Guide for the Care and Use of laboratory animals” and “Committee for Control and Supervision on experimental animals” (CPCSEA) to minimize pain and discomfort.

Immunohistochemistry

Cervical tissue taken from mice was put into formalin, then the fixation, washing, dehydration, clearing, infiltration, and embedding was carried out. Paraffin cervical tissue 4 µm thick was sliced with a microtome (Minux® Rotary Paraffin Microtomes, RWD Life Science Co., Ltd, USA). Tissue pre-treated with citric acid 0.01 M buffer solution (pH 6.0). Tissues were washed in PBS and then incubated with MMP-9, Glut-1, and IL-1β antibodies at 37°C before undergoing avidin-biotin-peroxidase treatment. Colorimetric visualization was performed using 3,3-diaminobenzidine (DAB) hydrochloride, followed by Mayer's hematoxylin staining. Cervical samples stained with

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**Table 1.** Value of MMP9 expression after given by *R. tomentosa* in carcinoma cervical histology.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean ± SD</th>
<th>Kruskal-Wallis</th>
<th>Mann-Whitney</th>
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</thead>
<tbody>
<tr>
<td>C-</td>
<td>6.22 ± 1.43</td>
<td>0.000</td>
<td></td>
</tr>
<tr>
<td>C+</td>
<td>17.00 ± 3.22***</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>8.67± 4.66**</td>
<td>0.040</td>
<td></td>
</tr>
<tr>
<td>MR100</td>
<td>11.77 ± 3.03*</td>
<td>0.040</td>
<td></td>
</tr>
<tr>
<td>MR200</td>
<td>8.97 ± 2.44**</td>
<td>0.040</td>
<td></td>
</tr>
<tr>
<td>MR400</td>
<td>7.02 ± 1.38**</td>
<td>0.040</td>
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</table>

C.: untreated; C+: cervical cancer; MR100: cervical cancer + 100 mg BW of *R. tomentosa*; C: vitamin C 0.2 mg/kg BW; MR200: cervical cancer + 200 mg BW of *R. tomentosa*; MR400: cervical cancer + 400 mg BW of *R. tomentosa*. *P<0.05 versus C-, ***P<0.001 versus C-, **P<0.01 versus C+. 

**RESULTS**

The analysis in Table 1, the Kruskal Wallis assessment, and the Mann-Whitney test demonstrate significant variations. The C+ group and the MR100, MR200, and MR400 groups exhibited substantially different levels of MMP9 expression, according to the average results (p<0.05 or p<0.01). The MMP9 expression level was highest in the C+ group and lowest in the C- group. The MR100 and MR200 treatment groups showed significant results when compared to C- (p<0.05), comparatively modest to the MR400 group. As a result, the C-group that received MR100 had very comparable results. The scattered carcinoma affected the pelvic surface, and there was no apparent boundary between the tumor and the pelvic surface. Furthermore, the tumor's center is irregular, in contrast to C-group histopathology, which revealed that the cervical tissue still consisted of normal tissue (Fig. 1A-B). Lesions were more severe at the MR100 dose compared to the C- and C+, but MMP9 expression started to decline (Fig. 1C). The herb was able to significantly reduce the expression of MMP9 at doses of 200 and 400 mg/kg BW by minimizing the distance between tumors, preventing the growth of the carcinoma, and allowing the nucleus to form appropriately (Fig. 1D-E). As a result, it was discovered that MR could enhance rat histology and reduce MMP9 expression in cervical cancer histology.

According to the mean value, there is a notable change with a p=0.00. There was not any real distinction in GLUT-1 expression between the C+ group given MRT100 at the dosage of 200 and 400 mg/kg BW (p<0.01) and the control group (p>0.05) (Table 2). The cervical cells of group C- had normal nuclei and epithelial lining on histology (Fig. 2A). The undifferentiated cells in Fig. 2B, on the other hand, were limited to the epithelium's bottom layers and showed signs of mitosis. Improved GLUT-1 expression and epithelial thickness are markers of lower epithelial cell abnormalities such as uncontrolled growth of cells, abnormal cell form, a substantial nucleus-cytoplasm percentage, and numerous nucleus structure modifications. GLUT-1 expression in cancer tissue was reduced with higher MR exposure. Immunohistochemistry results revealed reduced brown-stained nuclei after MR administration (Fig. 2C-E), a positive sign of GLUT-1 expression. The unmanageable tissue carcinomas of the untreated cancer group (C+) have paused and are no longer progressing, becoming epithelial. The most excellent MR dose (400 mg/kg BW) was discovered to decrease this molecule's appearance in carcinoma based on examining carcinoma tissue.

The Kruskal-Wallis test revealed substantial variations over all groups (Table 3). Compared to the C+, the IL-1β expression was significantly different (p<0.00) according to the Mann-Whitney test. There were substantial variations from the C+ at both the

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most minor MR dosages (100 mg/kg BW; p<0.05) and the highest MR doses (200 and 400 mg/kg BW; p<0.01). IL-1β expression was highest in the C+ group and lowest in the C- group. The red arrows indicate areas of the nucleus and the cytoplasm where brownish-black staining revealed positive IL-1β expression (Fig. 3). The elements of the cell most important for making a diagnosis are the cytoplasm and nucleus; the background and stroma are skipped over. The spread of microscopic cancer cells has affected lymph nodes nearby, which can only be seen under a microscope. The expansion of the nucleus (Fig. 3B-C), a significant ratio between the nucleus and the cytoplasm, irregular cell shape, uncontrolled cell proliferation, and numerous variants in the nucleus structure are all indications of malignant tumors. The nucleus turned black after MR imaging, the cell shape became asymmetrical, and the nuclear-to-cytoplasm proportion stabilized. The cervical histopathology of the tissues improved and was comparable to the Control group (Fig. 3D-E).

![Figure 1. MMP9 expression in carcinoma cervical.](image1)

C-: untreated; C+: cervical cancer; MR100: cervical cancer + 100 mg BW of R.s tomentosa; C: vitamin C 0.2 mg/kg BW; MR200: cervical cancer + 200 mg BW of R. tomentosa; MR400: cervical cancer + 400 mg BW of R. tomentosa. Red arrows: Positive expression. Magnification 40×.

![Table 2. Value of GLUT-1 expression after given by Rhodomyrtus tomentosa in carcinoma cervical histology.](image2)

<table>
<thead>
<tr>
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<th>Kruskal-Wallis</th>
<th>Mann-Whitney</th>
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<td>C-</td>
<td>6.12 ± 1.40</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>C+</td>
<td>17.00 ± 3.22**</td>
<td>0.001</td>
<td>0.010</td>
</tr>
<tr>
<td>C</td>
<td>7.01 ± 2.66**</td>
<td>0.040</td>
<td>0.060</td>
</tr>
<tr>
<td>MR100</td>
<td>11.77 ± 3.03*</td>
<td>0.040</td>
<td>0.060</td>
</tr>
<tr>
<td>MR200</td>
<td>8.97 ± 2.44**</td>
<td>0.040</td>
<td>0.060</td>
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<tr>
<td>MR400</td>
<td>7.02 ± 1.38**</td>
<td>0.040</td>
<td>0.060</td>
</tr>
</tbody>
</table>

C-: untreated; C+: cervical cancer; MR100: cervical cancer + 100 mg BW of R.s tomentosa; C: vitamin C 0.2 mg/kg BW; MR200: cervical cancer + 200 mg BW of R. tomentosa; MR400: cervical cancer + 400 mg BW of R. tomentosa. *P<0.05 versus C, **P<0.01 versus C, ***P<0.001 versus C, ****P<0.05 versus C+.
Figure 2. GLUT-1 expression in carcinoma cervical.
C-: untreated; C+: cervical cancer; MR100: cervical cancer + 100 mg BW of R. tomentosa; C: vitamin C 0.2 mg/kg BW; MR200: cervical cancer + 200 mg BW of R. tomentosa; MR400: cervical cancer + 400 mg BW of R. tomentosa. Red arrows: Positive expression. Magnification 40×.

Table 3. Value of IL-1β expression after given by Rhodomyrtus tomentosa in carcinoma cervical histology.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mean ± SD</th>
<th>Kruskal-Wallis</th>
<th>Mann-Whitney</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>C-</td>
</tr>
<tr>
<td>C-</td>
<td>3.02 ± 0.04</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>C+</td>
<td>14.49 ± 1.13**</td>
<td>0.001</td>
<td>0.070</td>
</tr>
<tr>
<td>C</td>
<td>5.04 ± 1.45**</td>
<td>0.001</td>
<td>0.030</td>
</tr>
<tr>
<td>MR100</td>
<td>10.80 ± 3.11*</td>
<td>0.001</td>
<td>0.070</td>
</tr>
<tr>
<td>MR200</td>
<td>10.67 ± 2.21*</td>
<td>0.001</td>
<td>0.070</td>
</tr>
<tr>
<td>MR400</td>
<td>8.42 ± 1.34**</td>
<td>0.001</td>
<td>0.070</td>
</tr>
</tbody>
</table>

C-: untreated; C+: cervical cancer; MR100: cervical cancer + 100 mg BW of R. tomentosa; C: vitamin C 0.2 mg/kg BW; MR200: cervical cancer + 200 mg BW of R. tomentosa; MR400: cervical cancer + 400 mg BW of R. tomentosa. *P<0.05 versus C-, **P<0.01 versus C-, ***P<0.001 versus C-, p<0.05 versus C+, *p<0.01 versus C+).

Discussion

According to the findings of this study, administering MR, especially at a dosage of 400 mg/kg BW, reduced MMP-9 appearance in cervical cancer histopathologic alterations. R. tomentosa’s minimal particle size is utilized to shape- and size-manipulate materials. Previous research has shown that R. tomentosa in nano size is 600.1 ± 135.8 nm (Situmorang et al., 2021). This site is not nanoparticles but micro-colloidal. Changing the extract to nano size or colloidal form has better permeability in penetrating cells than in the extract only (Ahmed et al., 2016). Antioxidants like anthocyanins, acyl phloroglucinol, flavonoids, tannins, and triterpenes found in R. tomentosa help guard against hypoxia and cell death (Vo and Ngo, 2019); the more severe the cervical neoplastic lesion, the more intense and numerous the MMP-9 immunohistochemistry positive staining. In cervical malignancies, MMP-9, essential for cancer growth, is expressed more immunohistochemically (Mondal et al., 2020). At the macroscopic level, cervical cancer can be polypoid or...
infiltrative. Unlike polypoid tumors, infiltrative tumors attack and harm the tissue structure around them. The thickness of the squamous epithelial layer is enlarged, with coarse chromatin and conspicuous nucleoli visible under a microscope. The ratio of active enzymes to natural inhibitors is crucial in the body's capacity to break down MMP (Gobin et al., 2019). The MMP9 inhibitors had no immediate antioxidant effects. MMP inhibitor therapy may be helpful by reducing oxidative stress indirectly (Garcia-Alloza et al., 2009). There is a strong correlation between MMP activation and antioxidant in vivo via oxidative stress, such as in cancer tissue. The molecular pathways activated point to a close connection between ROS production and antioxidant-related MMP activity in vivo (Garcia-Alloza et al., 2009). The therapeutic use of MMP inhibitors may be advantageous by lowering the oxidative stress linked to R. tomentosa in an indirect manner (Garcia-Alloza et al., 2009).

The metabolic and vascular needs of the tumor may be indicated by GLUT-1 expression in cancer, which may have therapeutic consequences for survival and treatment planning (Pragallapati and Manyam, 2019). Numerous research has been done to determine the prognostic value of GLUT1 in malignancies because of its significance in oncogenesis (Barbosa and Martel, 2020; Zambrano et al., 2019). In cancer cells, enhanced glucose metabolism may be linked to GLUT1 overexpression (Barbosa and Martel, 2020). Antioxidants have been shown to reduce toxic side effects during cancer treatment. The antioxidant intervention was created because rich in antioxidants, such as R. tomentosa, already related to efficient treating cancer with few side effects (Situmorang et al., 2021; Vo and Ngo, 2019). The current study also found that the powerful phenolic gingerol components have recently been identified as the main active components in ginger extracts that enhance GLUT-1 (Mao et al., 2019). Some herbs, like Zanthoxylum acahnotropium, contain antioxidants that reduce MMP-9, GLUT-1, and cell death in the body's tissues and blood vessels and repair cervical cancer tissue damage (p<0.01). GLUT-1 expression was reduced at the highest herbal dose as 400 mg/kg BW (Simanullang et al., 2022).

When rats are given MR, the interpretation of IL-1β, which also encourages the growth of cancer cells, is reduced. Innate immune cells in cervical tissue identify foreign objects not part of the host by signaling the release of inflammatory cytokines (Zhang et al., 2020). These immune cells require outside assistance, such as antioxidants, because they do not always function at their best. Biological
processes like oxidative stress, brought on by cells' lack of antioxidants, can cause various diseases (George and Abrahamse, 2020). In addition, DNA damage is a factor in the emergence and growth of cancer. Because antioxidants are now a standard treatment strategy, and cancer is closely related (George and Abrahamse, 2020; Gulcin, 2020). Chemotherapy and radiation therapies damage tissue irreversibly by destroying tumor cells through a process, and those therapies do not involve antioxidants (George and Abrahamse, 2020). The proper antioxidant inhibitors can help treat cancer successfully (Gulcin, 2020). The extracts from this plant also contain aryl chloroglucinol, flavonoids, tannins, and triterpenes, all of which have significant benefits for mending cells (Vo and Ngo, 2019). Also, it is discussed how rhodomyrtone, a bioactive compound present in its leaves, inhibits the malignancy of A431 epidermoid carcinoma cells (Tayeh et al., 2017). Furthermore, rhodomyrtone inhibited SW1353 cell migration, invasion, and metastasis, implying that it has antitumor properties and may be helpful in antitumor therapy (Tayeh and Watanapokasin, 2020).

The limitation of this study is only used cervical cancer rats; further research with human cancer cells by administering R. tomentosa can be developed for further, more comprehensive research and analysis of specific gene targets.

CONCLUSION

This study revealed that R. tomentosa administered to cervical tissue improved histology. Like the control group, it reduced the space between the tumors, slowed carcinoma growth, and decreased MMP9, GLUT-1, and IL-1β expression. R. tomentosa could be a potential source of bioactive compounds with cytotoxic or anticancer effects.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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