

Apoptosis resistance induced by cytokines in SW 982 culture was suppressed by red jasmine rice (*Oryza sativa* Linn.) crude extract

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Background Rheumatoid arthritis (RA) is associated with inflammation of the synovial membrane which results in an abnormal proliferation and resistance to the apoptosis process in synovial fibroblasts leading to synovial hyperplasia and joint destruction. Reversal of apoptosis resistance of fibroblasts in RA synovium is one of the targets for suppression of RA pathogenesis.

Objectives This study aimed to investigate the apoptosis-inducing effects of crude extract of red jasmine rice (CE) on proinflammatory cytokine-stimulated apoptosis resistance in a human synovial sarcoma cell line (SW982).

Methods SW982 cells were preincubated for 6 hours with combined cytokines, tumor necrosis factor- α (TNF- α), and interleukin 17-A (IL-17A). That was followed by the addition of CE at a concentration of 12.50-100 μ g/ml. After either 24 or 48 hours of incubation, expression of apoptotic related genes, including the FLICE-like inhibitory protein gene (*FLIP*), the anti-apoptotic gene (*Bcl-2*), and the pro-apoptotic gene (*Bax*), was determined by real-time PCR. Expression of the apoptotic cells was determined by flow cytometric analysis and the caspase-3 activity was analyzed by ELISA.

Results The expression of the apoptosis resistance markers, *FLIP* and *Bcl-2/Bax* ratio, was significantly elevated when the cells were treated with the combined cytokines compared with the control group. These markers were significantly decreased when co-treated with CE. These results were concomitant with a rise in caspase-3 activity and an increase in apoptotic cells when compared to the cytokine-treated group.

Conclusions CE reduces cytokine-induced apoptotic resistance in SW982 cells via down regulation of the expression of anti-apoptotic genes. These results suggest application of CE is an alternative treatment of RA. **Chiang Mai Medical Journal 2018;57(1):11-20.**

Keywords: rheumatoid arthritis, apoptosis resistance, red jasmin rice crude extract

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory joint disease, but the cause of the

disease is unclear. There is, however, substantial evidence that indicates the etiology of the

disease is associated with autoimmune disease. Inflammatory conditions occur throughout the body system of RA patients, especially at the articular capsules. The pathology of RA is associated with fibroblast-like synoviocyte cells which play a critical role in synovial membranes. The RA synovial fibroblast cells represent abnormal proliferation and resistance to the apoptosis process which leads to hyperplasia of the synovial membrane and pannus formation. Articular cartilage is infiltrated by synovial hyperplasia and demolished (1-7).

Various proinflammatory cytokines are involved in RA, including interleukin 1 beta (IL-1 β), interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-17 (IL-17) and tumor necrosis factor alpha (TNF- α). The inflammatory cells secrete a large quantity of proinflammatory cytokines in the RA condition. Previous studies have reported that TNF- α plays a critical role in the survival of RA synovial fibroblast (RASf) cells (8). Moreover, anti-apoptotic *Bcl-2* gene expression has been reported to be upregulated in RASf cells when the cells were incubated with IL-17A (9).

Presently, RA treatment is focused on medication and, in severe cases, joint replacement. Steroidal and nonsteroidal drugs are used for pain relief and as an anti-inflammatory. Dexamethasone is the primary choice for RA treatment (10,11). It was found that this drug induces the apoptosis process in pulmonary arterial smooth muscle cells and in human acute leukemia cell lines (12,13). However, previous studies have also found that the apoptotic induction of synovial fibroblast cells is induced by some medications (8,14). Statins, a class of lipid-lowering medications, have been found to induce apoptosis in RASf cells (14,15). Fluvastatin, a member of the statin drug class, has been reported to activate apoptosis in a human synovial sarcoma cell line (SW982), which are promoted cellular resistance to apoptosis by TNF- α (8). Moreover, natural substances such as gallic acid (16), norisoboldine (17), and lunasin (18), have been demonstrated pro-apoptotic effects in RASf cells (14,15). This indicates that apoptotic induction of RASf cells by natural products may represent a useful strategy for treatment of RA.

This study evaluated the apoptosis-inducing effects of red rice (red jasmine rice, *Oryza sativa* Linn.) crude extract (CE). Previous studies have reported the existence of many phytonutrients in red jasmine rice extract (19-21) including γ -oryzanol, tocopherols, tocotrienols, phenolic compounds, and proanthocyanidin. Several recent studies have shown that proanthocyanidin, γ -tocotrienol, and γ -oryzanol induce apoptosis in various types of cancer cells (22-28). However, the effect of red jasmine rice extract on induction apoptosis in RASf cells has not been reported. We hypothesized that red jasmine rice crude extract may have apoptotic induction effects on RASf cells. We investigated the apoptotic activating effects of CE against proinflammatory cytokine-induced apoptosis resistance in a SW982 cell line culture model. This research provides evidence that red jasmine rice extract is a potential alternative treatment for RA.

Methods

Chemicals and reagents

Leiboivitz's L-15 Medium, penicillin, streptomycin, gentamicin, and fetal calf serum (FCS) were purchased from Gibco-BRL (Grand Island, NY, USA). Tumor necrosis factor - α (TNF- α) and Interleukin-17A (IL-17A) were purchased from ProSpec Protein Specialist (Ness-Ziona, Israel). MTT 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) and dimethyl sulfoxide (DMSO) were purchased from Sigma-Aldrich (Louis, Missouri, USA). An RNAspin Mini RNA Isolation kit was purchased from GE Healthcare (Buckinghamshire, UK). A Revertra Ace[®] qPCR Rt kit was obtained from TOYOBO (Osaka, Japan). Commercial SYBR green I dye was purchased from Bio-Rad (Hercules, California, USA). An annexin-V-FLUOS staining kit was obtained from Roche Holding AG (Basel, Switzerland). A caspase-3 colorimetric activity assay kit was purchased from Merck Millipore (Burlington, Massachusetts, USA).

Preparations of crude red jasmine rice extract (CE)

The red jasmine rice crude extract (CE) was prepared as described in previous studies (20,21), i.e., the red jasmine rice was macerated in 80% ethanol followed by evaporation and lyophilization. The CE powder was then dissolved in dimethyl sulfoxide (DMSO) to form a stock solution which was then diluted to final concentrations in the culture media for each experiment.

Apoptosis resistance in the SW982 cell culture model

The human synovial sarcoma cell line SW982 (ATCC® Catalog No. HTB-93TM) was cultured in Leibovitz's L-15 medium supplemented with 10% fetal calf serum (FCS), 200 units/mL penicillin, 200 µg/mL streptomycin, and 50 µg/mL gentamicin at 37°C in an incubator with a 5% carbon dioxide atmosphere. SW982 cells were seeded in 6-well plates (2×10^6 cell/well). The cells were grown to 70-80% confluence and then stimulated for 6 hours with the combined cytokines, 10 ng/mL of TNF- α and 10 ng/mL of IL-17A, followed by the addition of CE at concentrations ranging from 12.5 to 100 µg/mL and incubation for a further 6 to 24 hours. Dexamethasone was used as the positive control. At the end of the incubation period, the cells were harvested for mRNA analysis.

Cell viability assay by MTT

SW982 cells were seeded in 96-well plates (2×10^4 cell/well) for 24 hours. The cells were incubated either with or without the cytokines for 6 hours after which CE at concentrations ranging from 0 to 100 µg/mL was added for an additional 24 and 48 hours. The control vehicle (DMSO) was prepared at the same time. At the end of the incubation period, the culture media was discarded. The MTT solutions were added to each well and incubated for 4 hours at 37°C. The formazan crystals were dissolved in DMSO. The absorbance was detected at 540 nm with a Thermo Scientific Multiskan® EX (28).

Quantification of apoptotic cells by flow-cytometric analysis

Apoptotic cells were detected by flow-cytometric analysis using Annexin-V-PI binding statistical analysis according to the manufacturer's instructions. SW982 cells were seed in 24-well plates (1.5×10^5 cells/well). The cells were grown to 70-80% confluence then stimulated with the combined cytokines for 6 hours, followed by the addition of CE at concentrations of 12.5, 25, 50, and 100 µg/mL. After either 24 or 48 hours of

incubation, the cells were collected and washed with phosphate buffer saline (PBS) prior to centrifugation at 500 x g for 5 minutes. The pellet cells were resuspended in 50 µL of Annexin-V- FLUOS labeling solution and incubated at 15 to 25°C for 10 to 15 minutes followed by the addition of 250 µL of incubation buffer. The apoptotic cells were analyzed by flow cytometry using a BD FACSCanto™ II system.

ELISA assay for caspase-3 activity

Caspase-3 activity was determined with a Caspase-3 Colorimetric Activity Assay Kit (MERCK Millipore) following the manufacturer's instructions. SW982 cells were seeded in 6-well plates (2×10^6 cells/well). The cells were stimulated with the combined cytokines for 6 hours prior to adding CE at concentrations of 25, 50, and 100 µg/mL. After 24 hours incubation, the cells were further incubated on ice with chilled 1x Cell Lysis Buffer for 10 minutes and then centrifuged at 10,000 x g for 5 minutes. The supernatant was then collected and protein concentration was measured. After that, the test samples were incubated with caspase-3 substrate for 1 hour at 37°C. Caspase-3 activity was measured at 405 nm with a Thermo Scientific Multiskan® EX.

Analysis of mRNA expression using real-time RT-PCR

The isolation of total RNA from harvested cells was done using an illustra RNAspin Mini Kit (GE Healthcare). cDNA was synthesized from 1.0 µg of the total RNA using a ReverTra Ace® qPCR RT Master Mix (TOYOBO) following the manufacturer's instructions. The reactions were prepared using specific primers and a SensiFAST™ SYBR® No-ROX kit. Detection in the mix samples was done using a Chromo4™ Four-Color Real-Time detector. The specific primers were selected based on the GenBank database (Table 1). All gene expressions were normalized with *GAPDH*. The results were obtained using a real-time PCR machine that performed the analyses using the $2^{-\Delta\Delta Ct}$ method (29).

Table 1. Primer sequences

Gene	Primer	Sequence (5'-3')	GenBank accession number
Bcl-2	Forward	TGTGTGTGGAGAGCGTCAA	NM_000633.2
	Reverse	GACAGCCAGGAGAAATCAAACAG	
Bax	Forward	AGCAGATCATGAAGACAGGGG	NM_001291428.1
	Reverse	ACACTCGCTCAGCTTCTTGG	
FLIP	Forward	TTTTGTGCCGGGATGTTGCT	NM_003879.5
	Reverse	GAGCAGGTCAAATCGCCTCA	
GAPDH	Forward	GAAGGTGAAGGTCGGAGTC	NM_002046.5
	Reverse	GAAGATGGTGATGGGATTTC	

Statistical analysis

Statistical analysis was done using One-Way ANOVA followed by multiple-comparison post-hoc correction. Results are expressed as mean $\pm$ SD for the three independent experiments. *p*-values <0.05 were considered statistically significant.

Results

Figure 1 shows the cytotoxic effect of CE on SW982 when co-treated with the combined proinflammatory cytokines. It was found that CE at 100 μ g/mL was able to reduce cell viability 81.35% and 58.52% following 24 and 48 hours of incubation, respectively

To quantify the apoptotic induction of CE in cytokine-induced apoptosis resistant SW982 cells, the apoptotic cells were analyzed with a Flow cytometer. As shown in Figure 2, the combination of proinflammatory cytokines did not increase the number of either early or late apoptotic cells after 24 or 48 hours of incubation when compared to the control (Figure 2B and 2D). In co-treatments with the cytokines and the CE for 24 hours, it was found that CE concentrations ranging from 12.5 to 100 μ g/mL significantly increased the number of early apoptotic cells which were up to 17.1% of the total (Figure 2B). At 48 hours of incubation, CE at a concentration of 100 μ g/mL significantly

elevated the number of early apoptotic cells by up to 21.3% of the total while only slightly inducing late apoptotic cells (Figure 2D). Dexamethazone as the control drug did not show induction activity in apoptotic cells at either 24 or 48 hours.

Caspase-3 activity was determined to confirm the apoptotic induction of CE in cytokine-induced apoptosis resistant SW982 cells. As shown in Figure 3, combination treatment with TNF- α and IL-17A did not affect caspase-3 activity when compared to the control. In co-treatments with the cytokines and CE, it was found that the extract at concentrations of 50 μ g/mL significantly activated caspase-3 activity when compared to the cytokines treatment group. However, dexamethazone did not induce caspase-3 activity (Figure 3).

In order to mimic apoptosis resistance in rheumatoid arthritis, the SW982 cell line was induced by the combined cytokines, TNF- α and IL-17A. It was found that the combined cytokines induced the expression of anti-apoptotic genes such as *Bcl-2* and *FLIP* while suppressing the pro-apoptotic gene *Bax* (Fig. 4A and 4C). These results were confirmed by a dramatic increase in the *Bcl-2* and *Bax* ratio (Figure 4B). Dexamethazone was found to suppress these activities. However, combination

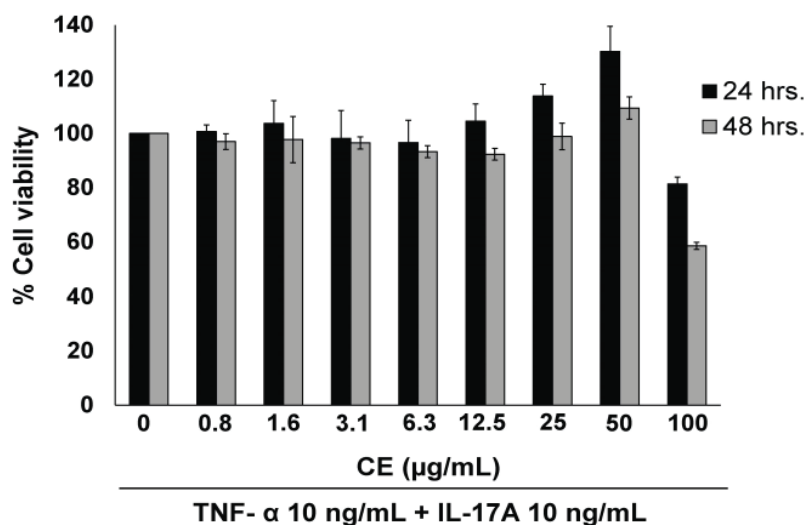


Figure 1. Effect of red jasmine rice crude extract (CE) on cell viability in cytokine-pretreated SW 982 culture. SW982 was pretreated with the combined cytokines for 6 hours followed by the addition of CE and incubation for either 24 or 48 hours. Cell viability was determined by MTT assay
C; untreated control, Dex; 10 nM dexamethasone

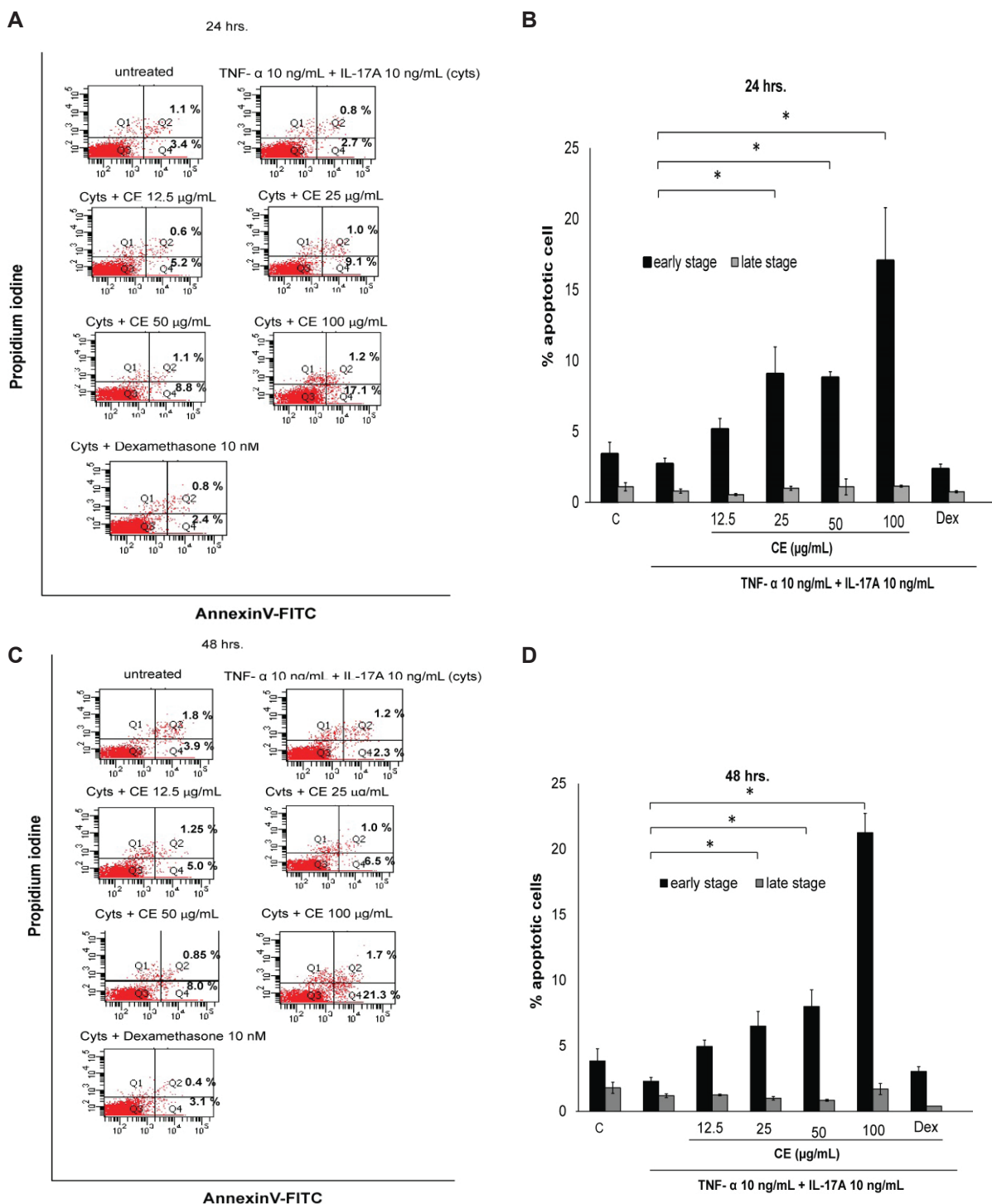


Figure 2. Effect of red jasmine rice crude extract (CE) on cell apoptosis in cytokine-pretreated SW 982 culture. SW982 was pretreated with the combined cytokines for 6 hours followed by the addition of CE and incubation for 24 to 48 hours. Apoptotic cells were assessed by Flow-cytometric analysis of annexin-V-PI binding

*; $p < 0.05$, C; untreated control, Dex; 10 nM dexamethasone

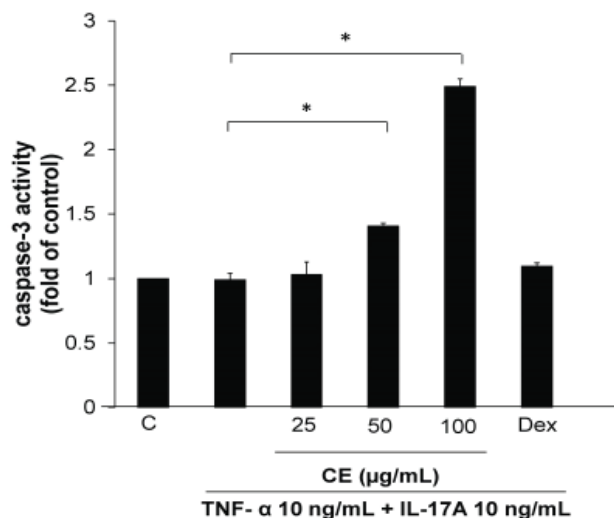


Figure 3. Effect of red jasmine rice crude extract (CE) on caspase-3 activity in cytokine-pretreated SW 982 culture. SW982 was pretreated with the combined cytokines for 6 hours followed by the addition of CE and incubation for 24 hours. Caspase-3 activity was analyzed by ELISA test kit. Results are expressed as mean $\pm$ SD of three independent experiments. *; $p < 0.05$, C; untreated control, Dex; 10 nM dexamethasone

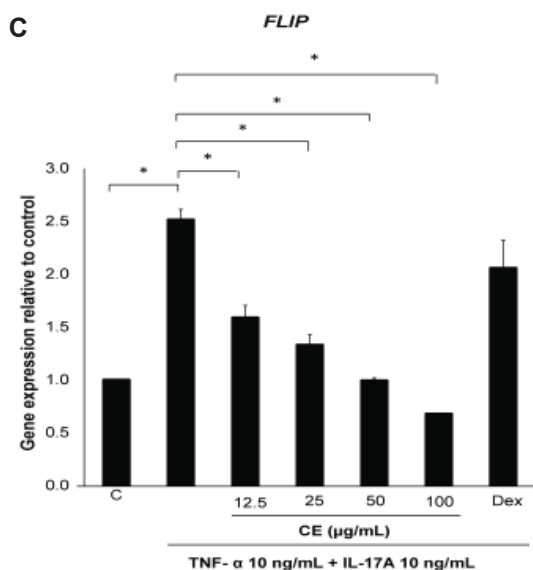
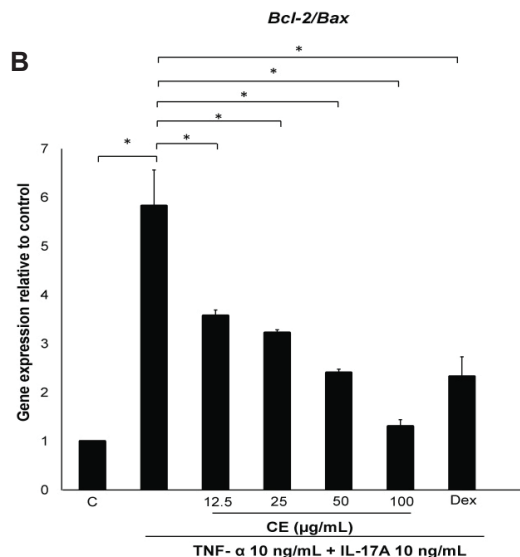
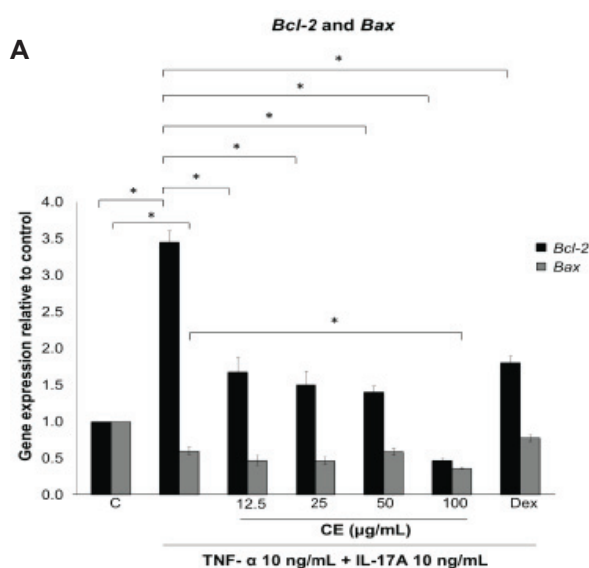


Figure 4. Effect of red jasmine rice crude extract (CE) on mRNA expression of apoptosis resistance markers *Bcl-2* and *Bax* (A), the ratio of *Bcl-2/Bax* (B) and *FLIP* (C). The SW982 cell line was pretreated with the combined cytokines for 6 hours followed by the addition of CE and incubation for 24 hours. Gene expression was assessed by real-time RT-PCR. Results are expressed as mean $\pm$ SD of three independent experiments. *; $p < 0.05$, C; untreated control, Dex; 10 nM dexamethasone

treatment with cytokines (TNF- α and IL-17) and crude extract (CE) (12.5 to 100 μ g/mL) significantly decreased *Bcl-2* and *FLIP* mRNA expression in a dose-dependent manner (Fig. 4A and 4C). These results were verified by the significant decrease in the ratio of *Bcl-2* and *Bax* (Figure 4B).

Discussion

Rheumatoid arthritis (RA) has been determined to be associated with synovial inflammation. The resident synovial cells, fibroblast-like synoviocytes, were found to be resistant to the apoptosis process and to unusual proliferation (1,6). Previous studies have reported that *Bcl-2*, *Bcl-XL*, and *FLIP* were highly expressed in synovial fibroblast cells of RA patients (30). *Bcl-2* is an anti-apoptotic protein that plays a role in the intrinsic pathway. It inhibits the dimerization of the pro-apoptotic *Bax* on the mitochondrial membrane (31,32). *FLIP* is an inhibitory protein that has a function in the extrinsic pathway. This protein inhibits the occurrence of the death-inducing signaling complex (DISC) (31). These expressions are involved in apoptosis resistance.

The present study found that *Bcl-2* and *FLIP* mRNA expression was significantly increased when the synovial sarcoma cell line (SW982) was treated with the combined proinflammatory cytokines, tumor necrosis factor- α (TNF- α), and interleukin-17A (IL-17A), which have been reported to be involved in RA pathogenesis. This indicates apoptosis resistance which mimics RA. A previous study reported that IL-17A induced *Bcl-2* gene expression in RA synovial fibroblast cells (9). It has been demonstrated that TNF- α -treated SW982 mimics RA synovial fibroblast cells (8). The synergistic effects of the combination of TNF- α and IL-17A have been reported in RA synovial fibroblast cells (33). These reports are consistent with our results. The gene expression of *Bcl-2* and *FLIP* are activated via the NF- κ B pathway by TNF- α and IL-17A induction (34). Although TNF- α is able to induce both apoptotic and survival pathways, that induction is dependent on the concentration of TNF- α and the a high level of expression of surviving proteins such as *Bcl-2*, *Bcl-XL*, *ICAP* and *XIAP* (35). Our

results show that IL-17A induces the expression of anti-apoptotic proteins in SW982 which drives TNF- α activated NF- κ B more than the apoptotic pathway. Dexamethasone, a drug of choice for RA treatment, was found to suppress the ratio of *Bcl-2* and *Bax* mRNA expression. Previous studies have reported that this drug was able to induce the apoptosis process in pulmonary arterial smooth muscle cells and in a human acute leukemia cell line (12, 13). This suggests that the present study was successful in inducing apoptosis resistance in the SW982 cell line by treatment with the combined proinflammatory cytokines.

Previous studies have reported that red jasmine rice crude extract inhibits the invasion of cancer cells and inflammation of macrophage cells via the NF- κ B pathway (19-21). However, the apoptotic effect of red jasmine rice crude extract in SW982 cells has not been investigated. The present study verified the apoptotic effect of crude red jasmine rice extract on SW982 cell culture to stimulate the conditions for resistance to apoptosis by the combined proinflammatory cytokines TNF- α and IL-17A. These results show that high expression of *Bcl-2* and *FLIP* was significantly suppressed by red jasmine rice crude extract in a dose-dependent manner. This which indicates that red jasmine rice crude extract has the potential to induce apoptosis via both intrinsic and extrinsic pathways. This is supported by the finding that red jasmine rice extract significantly induces caspase-3 activity in cytokine-treated SW982 culture. Caspase-3 is an effector caspase that is important in apoptotic pathways (31,36). However, the apoptotic effects of crude red jasmine rice extract on caspase-8 and caspase-9 expression should be investigated to classify the mechanisms of action on the intrinsic and extrinsic pathways. The number of apoptotic cells in the early stage consistently significantly increased the response to crude red jasmine rice extract in a dose-dependent manner, while in the late stage it induced at high concentration of crude red jasmine rice extract over an extended period of time. Almost 50% of the apoptotic cells were induced by 100 μ g/mL of the extract after a 48 hour incubation period. This agrees with

the 48 hours MTT assay which showed that the crude extract at a concentration of 100 µg/mL reduced the viability of SW982 by almost 50%. Although dexamethasone was found to inhibit the effect of cytokines on upregulating markers of apoptosis resistance including *Bcl-2* and *FLIP* mRNA expression, the drug did not eventually induce the number of apoptotic cells in this model. This indicates that CE and dexamethasone have different effects on cellular signaling against RA pathogenesis.

Important phytochemicals, including proanthocyanidin, γ-tocotrienol and γ-oryzanol, are reported to be major constituents of red jasmine rice crude extract (21). The structure of proanthocyanidin obtained from red jasmine rice extract has been previously found to resemble the proanthocyanidin isolated from grape seed (37). It has been reported that grape seed proanthocyanidin induces the apoptosis process in cervical cancer cells, pancreas cancer cells, and colon cancer cells by suppressing the anti-apoptotic proteins *Bcl-2*, *Bak-1* and *Bcl-XL* and by upregulating caspase-3, caspase-9 and *Bax* (22-24,28). On the other hand, hydrophobic compounds, including γ-oryzanol, have been shown apoptotic induction in prostate cancer cells. Moreover, tocotrienol also induces the apoptosis process by increasing caspase-3, caspase-8, and caspase-9 expression in breast cancer cells (25). Thus the major components, proanthocyanidin, oryzanol and γ-tocotrienol, may be involved in the apoptotic activities of red jasmine rice extract. Investigation of activity in partial purifications and in purified compounds should be conducted.

Taken all together, the present study reveals the anti-RA activities of red jasmine rice crude extract which may promote apoptosis of synovial resistant cells of RA leading to a reduction of unusual proliferation, hyperplasia, and pannus formation in RA synovium. These results suggest an advantage of alternative medicine in RA treatment.

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Conflicts of Interest

We have no conflict of interest.

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ภาวะต้านการตายแบบอะพอพโทซิสที่ถูกเหนี่ยวนำโดยสารไซโตไคน์ในเซลล์ SW982 เพาะเลี้ยงถูกยับยั้งด้วยสารสกัดหยาบจากข้าวหอมมะลิแดง

รุ่งนรี ใจธรรม, สุพิชชา ธงห้อย, ปฎิวัติ กองแดง, ศุภชัย ยอดศิริ, ศิริวรรณ องค์ไชย และ พรงาม ลัมตระกูล
ภาควิชาชีวเคมี คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

บทนำ โรคข้ออักเสบรูมาตอยด์เป็นโรคที่มีการอักเสบแบบของเยื่อหุ้มข้อ ส่งผลให้เซลล์ภายในเยื่อหุ้มข้อมีการแบ่งตัวที่ผิดปกติและต้านทานต่อกระบวนการตายแบบอะพอพโทซิส เยื่อหุ้มข้อจะหนาตัวขึ้น แทรกซึมเข้าไปในกระดูกอ่อน และเกิดทำลายข้อต่อในที่สุด ดังนั้นการทำให้เซลล์เยื่อหุ้มข้อที่ผิดปกติตายแบบอะพอพโทซิสจึงเป็นเป้าหมายสำคัญประการหนึ่งในการยับยั้งพยาธิสภาพของโรคข้ออักเสบรูมาตอยด์

วัตถุประสงค์ เพื่อศึกษาผลของสารสกัดข้าวหอมมะลิแดงต่อการเหนี่ยวนำการตายแบบอะพอพโทซิสในเซลล์มะเร็งเยื่อหุ้มข้อ (SW982) ที่ถูกกระตุ้นให้มีสภาวะต้านทานต่อกระบวนการอะพอพโทซิสด้วยไซโตไคน์ก่ออักเสบในโรครูมาตอยด์

วิธีการศึกษา บ่มเซลล์ SW982 นาน 6 ชั่วโมง ด้วยทูเมอร์เนคโคซิสแฟคเตอร์-แอลฟา (TNF- α) ร่วมกับอินเตอร์ลิวคิน-สิบเจ็ดเอ (IL-17A) จากนั้นบ่มต่อจนครบ 24-48 ชั่วโมงในภาวะที่ไม่มี/มีสารสกัดข้าวหอมมะลิแดงที่ความเข้มข้น 12.50-100 ไมโครกรัมต่อมิลลิกรัม ทำการทดสอบการแสดงออกของยีนที่เกี่ยวข้องกับการตายแบบอะพอพโทซิส ได้แก่ FLICE-like inhibitory protein gene (*FLIP*), anti-apoptotic gene (*Bcl-2*) และ pro-apoptotic gene (*Bax*) ด้วยวิธี real-time RT-PCR วิเคราะห์การทำงานของ caspase-3 โดยวิธี ELISA ด้วยชุดน้ำยาสำเร็จรูป และตรวจวัดจำนวนเซลล์ที่ตายแบบอะพอพโทซิสโดยวิธี flow cytometric analysis

ผลการศึกษา พบว่า การใส่ไซโตไคน์ก่ออักเสบทั้งสองชนิดร่วมกัน ทำให้เซลล์มีการแสดงออกของสารบ่งชี้ภาวะต้านทานต่อกระบวนการตายแบบอะพอพโทซิส เช่น ยีน *FLIP* รวมทั้งสัดส่วนของ *Bcl-2/Bax* เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติเมื่อเปรียบเทียบกับกลุ่มควบคุม แต่การแสดงออกของยีนดังกล่าวลดลงอย่างมีนัยสำคัญเมื่อมีสารสกัดข้าวหอมมะลิแดงอยู่ร่วมด้วยตั้งแต่ความเข้มข้นที่ 12.50 ไมโครกรัมต่อมิลลิกรัมขึ้นไป สอดคล้องกับการเพิ่มขึ้นของ caspase-3 activity และการเพิ่มจำนวนการตายของเซลล์แบบอะพอพโทซิสเมื่อเปรียบเทียบกับกลุ่มที่มีเฉพาะสารไซโตไคน์ก่ออักเสบ

สรุปผลการศึกษา การศึกษาในครั้งนี้แสดงให้เห็นว่า ภาวะต้านทานต่อกระบวนการตายแบบอะพอพโทซิสของเซลล์ SW982 ที่เกิดจากการถูกกระตุ้นด้วยไซโตไคน์ สามารถถูกเหนี่ยวนำให้ตายได้โดยสารสกัดข้าวหอมมะลิแดงผ่านกลไกการลดการแสดงออกของยีนที่เกี่ยวข้องกับภาวะต้านทานต่อกระบวนการตายแบบอะพอพโทซิส ข้อมูลนี้จึงอาจเป็นประโยชน์ต่อการพัฒนาสารสกัดข้าวหอมมะลิแดงเพื่อเป็นการรักษาทางเลือกสำหรับโรคข้ออักเสบรูมาตอยด์ต่อไป *เชียงใหม่เวชสาร* 2561;57(1):11-20.

คำสำคัญ: ข้ออักเสบรูมาตอยด์ การต้านทานต่อกระบวนการตายแบบอะพอพโทซิส สารสกัดข้าวหอมมะลิแดง