TNF- α , IL-8, MCP-1, MIF were detected by ELISA method. Western blot method was used to detect the expression of MyD88, NF- κ B, ASC, and Caspase-1 in macrophages.

Results: The expression level of MyD88, NF- κ B, ASC and Caspase-1 protein in macrophages of model group was significantly up-regulated, and the levels of IL-1 β , TNF- α , IL-8, MCP-1, MIF and NO in the supernatant is increased significantly. TGP, SIN, TGP +SIN and Colchicine group compared with the model group, the expression of NF- κ B, MyD88, ASC, Caspase-1 protein in macrophage and the level of IL-1 β , TNF- α , IL-8, MCP-1, MIF and NO in supernatant were significantly decreased, the difference was statistically significant ($p < 0.05$). TGP +SIN group compared with Colchicine group, the expression of inflammatory pathways proteins and the levels of inflammatory cytokines were no difference ($p > 0.05$) (table 1).

Abstract AB0085 – Table 1. Expression of major inflammatory cytokines and signalling pathway proteins(X $\pm$ S)

Group	N	IL-1 β (pg/ml)	TNF- α (pg/ml)	MCP-1(pg/ml)	N	MyD88	NF- κ B
Control	9	60.258 ± 5.159	330.962 ± 15.046	196.222 ± 17.696	3	0.374 ± 0.017	0.413 ± 0.059
Model	9	115.360 $\pm 8.027^*$	638.118 $\pm 31.297^*$	568.332 $\pm 41.052^*$	3	0.831 $\pm 0.020^*$	0.871 $\pm 0.053^*$
Colch	9	78.561 $\pm 4.645^{\#}$	391.539 $\pm 21.616^{\#}$	339.777 $\pm 27.326^{\#}$	3	0.573 $\pm 0.024^{\#}$	0.568 $\pm 0.012^{\#}$
SIN	9	86.842 $\pm 5.758^{\# \Delta}$	461.174 $\pm 33.014^{\# \Delta}$	383.103 $\pm 26.296^{\# \Delta}$	3	0.674 $\pm 0.029^{\# \Delta}$	0.674 $\pm 0.012^{\# \Delta}$
TGP	9	93.200 $\pm 4.717^{\# \Delta \circ}$	466.507 $\pm 28.218^{\# \Delta \circ}$	421.988 $\pm 39.226^{\# \Delta \circ}$	3	0.699 $\pm 0.042^{\# \Delta \circ}$	0.777 $\pm 0.015^{\# \Delta \circ}$
SIN	9	79.902 $\pm 5.499^{\#}$	405.834 $\pm 20.824^{\#}$	343.728 $\pm 26.328^{\#}$	3	0.613 $\pm 0.026^{\#}$	0.575 $\pm 0.014^{\#}$

Note: * $P < 0.05$ vs Control; # $p < 0.05$ vs Model; $\Delta p < 0.05$ vs Colchicine; $\circ p < 0.05$ vs SIN

Conclusions: The anti-inflammatory effect of Chinese herbal extracts (TGP and SIN) on the multiple targets of the inflammatory model may be one of its mechanisms of action for the prevention and control of acute gout flares.

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Cartilage, synovium and bone

AB0086

TYPE II COLLAGEN AND GLYCOSAMINOGLYCAN TURNOVER IN BOVINE ARTICULAR CARTILAGE IS MODULATED BY LONG-TERM DYNAMIC COMPRESSION

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Background: Osteoarthritis (OA) patients suffer from progressive degradation of articular cartilage, to which there is no available treatment to block or reverse the catabolic mechanisms. Articular cartilage confers a biomechanical function in the joints, and in concordance chondrocytes have shown to be mechanosensitive. The effect of dynamic compression on cartilage extracellular matrix (ECM) could prove to be crucial for translational research in development and screening of new OA drug candidates.

Objectives: This study investigates the effect of long-term dynamic compression of a bovine articular cartilage *ex vivo* model through quantification of cartilage associated biomarkers.

Methods: Full depth bovine cartilage explants were cultured for 2 weeks. The explants were treated 3 times a week with either OSM [10 ng/mL] and TNF- α [2 ng/mL] (O+T), or TGF- β 1 [50 ng/mL]. Untreated samples were included as negative controls (w/o). For each condition two groups were established; an unloaded group and a group compressed 3 times a week. Compression was applied using Electroforce 5500 (TA Instruments), in a sine wave with a maximum load per cycle of 1 MPa, at 1 Hz frequency for 1200 cycles. Metabolic activity was measured once a week using AlamarBlue. Biomarkers released to the supernatant were assessed using the following well-described ELISAs: formation of type II collagen was measured by ProC2, and MMP-degradation of type II collagen was

measured by C2M. Sulfated glycosaminoglycans (sGAG) released to media, and sGAG extracted from the explants on the last day using a 4 mM GuHCl solution were quantified using a 1.9-dimethylmethylene blue (DMB) assay.

Results: Compression of bovine explants significantly decreased release of C2M compared to unloaded samples in O+T and w/o groups with 42% and 48% respectively. ProC2 release was not affected by compression. Compression of w/o or TGF- β treated explants increased sGAG release with 195% and 152% relative to their unloaded controls. However, the total amount of sGAG extracted from the explants on the last day remained unchanged. Compression of the explants did not affect the metabolic activity.

Abstract AB0086 – Figure 1

Conclusions: Compression significantly reduced the degradation of type II collagen, which in combination with unaltered formation as measured by ProC2, may suggest suppression of the involved catabolic processes and increased deposition of type II collagen in the cartilage matrix. Furthermore, compression elevated the sGAG release without reduction in the explant GAG content, indicating an increased turnover of GAG. In conclusion, the cartilage ECM turnover is significantly modulated by dynamic compression. This method adds essential translational value to the continuous research addressing OA.

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AB0087

SYNOVIAL TISSUE MACROPHAGES POLARISATION (M1, M2) IN PATIENTS WITH UNDIFFERENTIATED ARTHRITIS MEETING DIAGNOSTIC CRITERIA FOR RHEUMATOID ARTHRITIS OR PSORIATIC ARTHRITIS ALONG THE FOLLOW UP

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Background: Undifferentiated arthritis (UA) is defined as an inflammatory oligo- or polyarthritis that does not fulfil criteria for a definitive diagnosis. Earlier diagnosis would permit a better functional prognosis. Synovial tissue (ST) macrophages have been associated with disease activity, radiographic erosion and response to therapy in RA. Furthermore, it has been reported that M1 polarised macrophages predominate in RA synovitis, whereas M2 predominate in SpA synovitis.¹

Objectives: To analyse polarised macrophages (M1 proinflammatory and M2 anti-inflammatory) in ST of patients with UA which evolved to RA or PsA, after a long follow-up, to explore their diagnostic value.

Methods: To determine the polarisation state of macrophages in ST obtained by arthroscopy from patients with UA that evolved to RA (UA-RA=8) or PsA (UA-PsA=9), the expression of proteins associated to GM-CSF-driven polarisation M1 (INHBA, TNF α and MMP12) and M-CSF-driven polarisation M2 (CD209) was assessed in ST CD163⁺ macrophages. Patients with established RA (n=12) or PsA (n=10) were included as control. 4 μ m cryosections of ST in OCT were blocked for 10 min with 1% human immunoglobulins and incubated with primary (1–5 μ g/ml) and secondary antibodies. Imaging was performed with an inverted confocal microscope (SPE, Leica Microsystems) and glycerol immersion objective (ACS-APO 20x/NA 0.60). Single cell mean fluorescence intensity (MFI) was

assessed using ImageJ software (National Institutes of Health, Bethesda, MD, USA). At least three random fields were evaluated for each type of ST, quantifying the expression of INHBA, TNF- α , MMP12 and CD209 in all segmented CD163⁺ macrophages. Macrophages density was normalised based on selected tissue area (mm²). After background subtraction, data were plotted using Graph-Pad software (GraphPad Software, La Jolla, CA, USA).

Results: CD163⁺ sublining (SL) macrophages from UA-RA expressed abundantly the INHBA-encoded activin A, whereas TNF α and MMP12 were variably detected. Regarding the M-CSF-associated marker CD209, 2 populations of CD163⁺ macrophages were found in the SL of UA-RA, CD163⁺CD209⁺ and the other CD163⁺CD209⁻, with higher than 100 arbitrary units (au) for CD163⁺CD209⁺ and lower than 100 au for CD163⁺CD209⁻. Similarly, INHBA, MMP12 and TNF α expression and 2 populations of CD209 were detected in CD163⁺ macrophages from UA-PsA. Macrophage density was also found comparable between UA, with 650/mm² in UA-RA and 649/mm² in UA-PsA. Quantification of the above indicated markers in CD163⁺ST macrophages from established RA and PsA revealed similar levels of INHBA, TNF α , MMP12 and CD209 than those from UA-RA and UA-PsA.

Conclusions: This study shows for the first time that the polarisation state of ST CD163⁺ macrophages in UA progressing to RA and PsA is similar to that of established RA and PsA in terms of INHBA, MMP12, TNF α and CD209 expression. Therefore, the inflammatory polarisation state of macrophages is similar in RA and PsA and it is already detected at the earlier steps.

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AB0089

HISTOPATHOLOGICAL CHANGE CAUSED BY BIOLOGICAL TREATMENT IN RHEUMATOID ARTHRITIS SYNOVIAL TISSUE

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Background: Multiple studies addressing the effects of biologics on the synovial tissue in rheumatoid arthritis (RA) patients have been reported. There are, however, few studies comparing histopathological changes in the synovial tissue in the same RA patients between before and after biologics treatment.

Objectives: We examined biologics impacts on RA synovial tissues based on pathological findings in them collected during surgeries for the same patient before and after biological drug usage.

Methods: Synovial tissues were collected from 34 RA joints before and after biologics. The average age and disease duration of the study subjects were 64.0 and 22.5, respectively. Synovial tissues were evaluated by hematoxylin. Histopathological changes in the synovial tissues were compared based on Rooney's score, and presence or absence of fibrinoid degeneration and proliferation of villi in the subsynovial tissue. We examined correlation between pathological findings in RA synovium and disease activity under biologics. Disease activity was assessed by CDAI. We examined the Histopathological changes in the Remission, Low disease activity group (RL group) and Moderate disease activity (M group). Etanercept, Infliximab, Tocilizumab, Adalimumab and Abatacept was used as biological drug for 18, 6, 5, 3 and 2 joints respectively.

Results: Rooney score between before and after biological usage improved from 28.4 to 12.0 showing significant difference. Significant improvement in Rooney score was observed in all items. Fibrinoid degeneration was observed in 29 cases (85.3%) and 6 cases (17.6%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. Proliferation of villi was observed in 32 cases (94.1%) and 11 (32.4%) before and after biologics treatment, respectively, demonstrating a significant reduction with biologics treatment. After biologics treatment, Rooney's score in RL group and M group were 10.4 and 15.3, respectively, showing a statistically significant difference. In addition, the M group had significantly higher scores in lymphoid follicle and lymphocyte infiltration compared to the RL group.

Conclusions: The study results demonstrated that biologics treatment significantly ameliorated inflammatory changes in the synovial lining layers and sublining layers. In addition, the results suggested that histopathological findings in the sublining layers reflected disease activity.

Disclosure of Interest: None declared

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AB0090

VERBASCOSIDE AND HYDROXYTYROSOL DOWNREGULATE STRESS-RELATED PATHWAYS IN HUMAN OSTEOARTHRITIC ARTICULAR CHONDROCYTES

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Background: Osteoarthritis (OA), is a leading cause of joint dysfunction and the disease is characterised by progressive destruction of the articular cartilage.¹ At the molecular level, degeneration of the cartilage is attributed to multifactorial events including oxidative stress, mitochondrial dysfunction, apoptosis and associated changes in inflammatory and catabolic gene expression.² Recent studies have revealed the essential role of plant-derived antioxidants in preventing pathological events observed in joint diseases by modulating redox signalling.³

Objectives: Here, we studied whether the polyphenolic compounds verbascoside and hydroxytyrosol exert chondroprotective effects by suppressing oxidative stress pathways and IL-1, IL-1 β -converting enzyme (ICE) expression in human OA chondrocytes.

Methods: Chondrocytes were isolated from the joint cartilages of OA patients (grade 3–4) during total knee arthroplasty with the approval of Kecioren Training and Research Hospital, Clinical Research Ethics Committee (B.10.4.İSM.4.06.68.49), as described previously.⁴ The alterations in cell counts, viability (MTT, NRU), proliferation (RTCA-iCELLigence System), reactive oxygen species (ROS) generation, stress-related signalling proteins and inflammatory progenitors ICE/caspase-1 (ELISA) were determined.

Results: Cell viability was increased at lower concentrations of hydroxytyrosol in OA chondrocytes (P1, 30th day). On the other hand, verbascoside treated cells did not show any difference in the activity of mitochondrial oxidoreductases by the MTT assay. However, both polyphenols significantly increased proliferation and reduced intracellular ROS generation in OA chondrocytes at lower concentrations. Although verbascoside has no effect on ICE/caspase-1, treatment with hydroxytyrosol downregulated ICE/caspase-1, indicating a potential anti-inflammatory effect. Both polyphenols modulated the activation of stress activated signalling pathways via p38 and JNK proteins.

Conclusions: At low concentrations the antioxidants hydroxytyrosol and verbascoside may have potential chondroprotective effects in OA.

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AB0091

MECHANICAL EXPOSURE AND DIACEREIN TREATMENT MODULATES INTEGRIN-FAK-MAPKS MECHANOTRANSDUCTION IN HUMAN OSTEOARTHRITIS CHONDROCYTES

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Background: Progression of osteoarthritis (OA) is characterised by destruction of articular cartilage, thickening of subchondral bone, and formation of osteophytes. The disease modifying OA drug (DMOAD) diacerein functions as a slow acting drug through anti-inflammatory, anti-catabolic, and pro-anabolic effects on cartilage and the synovial membrane. Mechanical loading of joint tissue directly affects the homeostasis of matrix degrading enzyme production and matrix repair.