



## ABSTRACT

Chronic inflammation underpins many immune-related diseases, driving the need for functional foods with anti-inflammatory properties. This study developed a semi-soft goat cheese using Indonesia's indigenous starter culture Dad13-11 (*Lactiplantibacillus plantarum* subsp. *plantarum* Dad-13 and *Streptococcus thermophilus* Dad-11) and evaluated its anti-inflammatory effects. The development of cheese using indigenous starter cultures is crucial for ensuring ingredient sovereignty, reducing dependency on commercial cultures, and promoting local microbial diversity. The probiotic cheese met food standards with 7.98 Log CFU/g probiotic counts. The indigenous mixed starter cultures Dad13-11 demonstrated potential to outperform commercial starters by achieving higher lactic acid bacteria counts and greater efficiency in reducing pH and time during cheesemaking, while maintaining comparable physicochemical properties to the control cheese. Water extracts from the interior (CID) and rind (CRD) of probiotic cheese made with Dad13-11 starter, as well as the control interior of commercial starter culture (CIF), were tested on lipopolysaccharides (LPS)-stimulated RAW264.7 cells. CID suppressed interleukin-6 (IL-6) and nitric oxide (NO) production more effectively than CIF, while CRD showed the strongest activity, attributed to the rind's microbial complexity. Gene expression analysis confirmed CRD's superior downregulation of IL-6 and iNOS, followed by CID and CIF. Interestingly, MAPK and NF-κB assays showed higher suppression by control group (CIF and CRF), likely due to its stronger inhibition of upstream nuclear translocation. In contrast, probiotic group (CID and CRD) targeted downstream mechanisms, such as transcription co-factors and cytokine gene activity, explaining their greater cytokine suppression. Temporal differences between assays further clarified these contrasting results. These findings suggest that goat cheese made with Dad13-11 starter offers significant anti-inflammatory potential, with CRD being particularly effective, highlighting its application for managing chronic inflammation and immune disorders. The study underscores the importance of utilizing indigenous cultures to develop functional foods that contribute to local sovereignty in food production and the promotion of health benefits.

**Keywords:** anti-inflammation activity; cytokines; goat cheese; probiotic; MAPKS; NF-κB signaling pathway



## INTISARI

Peradangan kronis mendasari banyak penyakit terkait sistem imun, mendorong kebutuhan akan pangan fungsional dengan sifat anti-inflamasi. Penelitian ini mengembangkan keju kambing semi-lunak menggunakan kultur starter asli Indonesia Dad13-11 (*Lactiplantibacillus plantarum* subsp. *plantarum* Dad-13 dan *Streptococcus thermophilus* Dad-11) dan mengevaluasi efek anti-inflamasinya. Penggunaan kultur starter asli penting untuk mendukung kedaulatan bahan baku, mengurangi ketergantungan pada kultur komersial, dan mempromosikan keanekaragaman mikroba lokal. Keju probiotik yang dihasilkan memenuhi standar pangan dengan jumlah probiotik 7,98 Log CFU/g. Kultur starter Dad13-11 menunjukkan potensi mengungguli kultur komersial dengan mencapai jumlah bakteri asam laktat lebih tinggi, efisiensi lebih besar dalam menurunkan pH, dan waktu pembuatan keju lebih singkat, sementara mempertahankan sifat fisiko-kimia yang sebanding dengan keju kontrol. Ekstrak air dari bagian dalam (CID) dan kulit (CRD) keju probiotik Dad13-11, serta bagian dalam keju kontrol (CIF), diuji pada sel RAW264.7 yang distimulasi lipopolisakarida (LPS). CID lebih efektif menekan produksi interleukin-6 (IL-6) dan nitrit oksida (NO) dibandingkan CIF, sementara CRD menunjukkan aktivitas anti-inflamasi terkuat, diduga karena kompleksitas mikroba pada kulit keju. Analisis ekspresi gen mengonfirmasi bahwa CRD paling efektif menurunkan ekspresi IL-6 dan iNOS, diikuti oleh CID dan CIF. Uji MAPK dan NF-κB menunjukkan penekanan lebih kuat oleh kelompok kontrol (CIF dan CRF), kemungkinan karena inhibisi translokasi nuklir hulu. Sebaliknya, kelompok probiotik (CID dan CRD) menargetkan mekanisme hilir, seperti ko-faktor transkripsi dan aktivitas gen sitokin, yang menjelaskan penekanan sitokin yang lebih besar. Perbedaan temporal antara uji memperjelas hasil yang kontras ini. Temuan ini menunjukkan bahwa keju kambing dengan starter Dad13-11 memiliki potensi anti-inflamasi signifikan, terutama CRD, sehingga berpotensi diaplikasikan untuk mengelola peradangan kronis dan gangguan imun. Penelitian ini menegaskan pentingnya pemanfaatan kultur asli dalam pengembangan pangan fungsional untuk mendukung kedaulatan pangan dan memberikan manfaat kesehatan.

**Keywords:** anti-inflamasi; sitokin; keju kambing; probiotik; MAPKS; NF-κB signaling pathway