Introduction: Caryocar coriaceum Wittm (Caryocaraceae) is a tree popularly known in the Brazilian Northeast as "Pequi". Fixed oil from fruits of C. coriaceum (FOCC) has been extensively used in folk medicine for the treatment of cutaneous and sistemic inflammatory diseases. However, there are limited search for the topical anti-inflammatory effect. Dermatitis are multifactorial diseases where inflammatory response has a central role, and the actual pharmacotherapy for the treatment of it has not been effective or have limitations. So, the aim of the present study was to evaluate the anti-inflammatory effect of FOCC in an experimental model of irritant contact dermatitis induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) in mice. Methods: The FOCC was obtained by mechanical extraction under discontinuous hydraulic pressing and characterized by GC/MS and CG-FID. The study was approved by the Ethics Committee on Animal Use of the Federal University of Ceará (4876091118). The Swiss mice (20-30g) were treated with FOCC (100, 200 and 400 mg/kg, p.o.), aqueous solution of DMSO 1% (control group) or dexamethasone (standard drug, 1mg/kg, p.o.) 1 hour before the administration of TPA (2.5 µg/ear-10 µl). Ear thickness was recorded before and 4 hours after TPA administration using a digital caliper. The animals were sacrificed, and ear tissue homogenate were prepared and used for the determination of myeloperoxidase (MPO) activity and cytokine levels (TNF- α and IL-10). Statistical analysis was performed (GraphPadPrism 6.0-USA) and the results are expressed as mean \pm S.E.M. The comparison between the means was performed using analysis of variance (ANOVA) followed by Tukey's test (p <0.05). **Results:** Chemical analysis of FOCC identified ten fatty acids being 60.6 % of unsatured fatty acids and 39 % saturated fatty acids. The oleic and palmitic acids are the majoritary constituents. Oral pretreatment of mice with FOCC (200 and 400 mg/kg) significantly reduced the ear edema (61% and 64% inhibition, respectively) induced by TPA when related to control group. The administration of TPA significantly increased MPO activity (1.29 ± 0.1) when related to untreated group (0.21 ± 0.05) , and this effect was significantly reduced by of OFCC

 (0.33 ± 0.1) . In addition, the FOCC suppressed the TNF α levels (77.61 ± 5.7 pg/mL) when related to TPA treated group (121.8 ± 7.7 pg/mL) and prevented the increase of the IL-10 levels (102.3 ± 7.0 pg/mL) similar to dexamethasone group (108.8 ± 13,1 pg/mL). **Conclusion:** This is the first experimental study which determined the cutaneous anti-inflammatory activity of FOCC in irritant contact dermatitis model in mice. The FOCC showed an antiedematogenic effect acting in the accumulation of leukocyte and modulating the pro- and anti-inflammatory cytokines levels. These findings suggest that FOCC is a promising bioactive fixed oil being good candidates for drug development for the treatment of cutaneous inflammatory diseases.