Biological activities of the gelam honey- a review paper


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Abstract

Honey has been used for the different biological activities. It has the ability to treat and control various kinds of diseases. The usage of honey as the natural sources is from the ancient time because of its safe usage. In the present review the important applications of honey are clarified for the beneficial purpose of people all over world and especially Gelam honey is discussed in this review.

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Introduction

The utilization of regular sources in treating malignancy turns out to be progressively unmistakable these days. Promising information from research uncovered its natural exercises particularly on human wellbeing. Honey is one of the potential applicants. Honey has been expended since antiquated time. Assortment of sugars, flavonoids, phenolic acids, chemicals, amino acids, proteins, and different mixes can be found in Honey (Hussain et al., 2011; Hussein et al., 2012). The arrangement of Honey more often than not relies upon the blossoms devoured by bumble bees and ecological elements. In this manner, the fundamental concentrated in this audit is on Gelam Honey which was collected from Gelam backwoods. Gelam Honey generally inception from Terengganu, Malaysia as it has abundantly of Gelam backwoods (Moniruzzaman et al., 2013). The Gelam or Melaleuca is an individual from the Myrtaceae family with answered to have the properties, for example, calming (Liu et al., 2005), anticancer (Wolter et al., 2002), hepatoprotective (Saravanan et al., 2006), and anthelmintic exercises (Johari et al., 2019). Subsequently, the audits on logical examinations were required on the organic exercises of Gelam Honey, which later can be utilized in the advancement of elective common based treatment drugs.

Gelam honey and it’s uses

Gelam honey as an antimicrobial

Honey is settled for its strong antimicrobial action against various kinds of microscopic organisms. These incorporate Acinetobacter baumannii, Enterobacter aerogenes, vancomycin-safe Enterococcus faecium, cotrimoxazole-safe Escherichia coli, Haemophilus influenzae, Klebsiella oxytoca, Klebsiella pneumoniae, ciprofloxacin-safe Pseudomonas aeruginosa, Salmonella sp. (S. california, S. enteridis,furthermore, S. typhimurium), methicillin-safe Staphylococcus aureus (MRSA), and various multidrug-safe bacterial disengages (Szeweda et al., 2017). Factors, for example, causticity levels (low pH), osmotic weight, hydrogen peroxide (H₂O₂) content just as the nearness of non-peroxide segments, for instance, methylglyoxal may add with this impact. What's more, changing degrees of antimicrobial properties of Honey additionally have been credited to topographical inconsistencies, flower sources and the centralization of Honey utilized in specific medications (Mandal et al., 2011). With respect to Gelam Honey, a few examinations have been performed to assess its antimicrobial impact against chosen bacterial strains. (Zainolet al., 2013) played out a similar investigation of the antibacterial movement of Gelam Honey other than other Malaysian Honeys (acacia, Kelulut, pineapple, and Tualang) against S. aureus, Bacillus cereus, E. coli, and P. aeruginosa. Examination of results demonstrated that Gelam Honey had the least inhibitory focus (MIC) and least bactericidal fixation (MBC) values, at 5% (w/v) and 6.25% (w/v), individually, against S. aureus contrasted and other bacterial secludes. Pineapple Honey, then again, was required at a most noteworthy focus to repress and wipe out E. coli and P. aeruginosa with the MIC and MBC values at 25% (w/v) and half (w/v), individually. In the agar restraint examine, Gelam Honey exhibited most elevated antibacterial action against B. cereus with 23.04 comparable phenol fixations (EPC) and non-peroxide movement of 22.31 EPC. Additionally, acacia Honey has been appeared to have most minimal antibacterial movement against E. coli with an all-out EPC action and non-peroxide EPC action of 7.85 and 7.59, individually. Taken together, results from this investigation suggest that bacterial disposal by Honey happened at a fixation needy and microbial-subordinate habits in which Gelam Honey was observed to be a powerful antibacterial operator against S. aureus and B. cereus (Zainol et al., 2013). Both S. aureus and B. cereus are among the major pathogenic microscopic organisms which can cause different hazardous contaminations in human (Bottone et al., 2010; Tong et al., 2015).

In the accompanying investigation, Gelam, Tualang, and Durian Honeys were tried for their development inhibitory exercises against S. aureus, S. epidermidis, E. coli, Salmonella enterica serovar Typhimurium, K. pneumoniae, and vancomycin-safe enterococci (E.
It was exhibited by the outcomes that Gelam Honey had better inhibitory action thought about than Tualang Honey at the fixation began from 40% v/v of undiluted Honey. It was compelling against every tried bacterium with the MIC and MBC qualities extending from 125–1000 mg/mL to 125–2000 mg/mL, separately. Also, Durian Honey displayed the weakest antibacterial impact and subsequently positioned third contrasted with Tualang and Gelam Honey at the second and first position, individually, for their power as antibacterial operator (Ng et al., 2014). In an ongoing report, Ng and accomplice tried the counter staphylococcal impact of Gelam Honey utilizing S. aureus methicillin-delicate (MSSA) and methicillin safe (MRSA) strains. In view of the outcomes, they found that Gelam Honey at 80% (v/v) applied most astounding bacterial development restraint in the two strains, almost like that of undiluted Honey. The impact was hypothesized to be because of the high thickness of Honey which controls the dispersion of bactericidal substances (Ng et al., 2015). Biofilm is described by the presence of a populace of cells that join irreversibly on various biotic and abiotic surfaces and encased in a hydrated grid of exopolymeric substances, proteins, polysaccharides, and nucleic acids (Mohamed et al., 2007). Biofilm has been involved with 80% of human bacterial diseases, which, causes the tinted zone impervious to antimicrobial operators (Römling et al., 2012). Enterococci, especially E. faecium and E. faecalis have been distinguished as the third significant reason for nosocomial contamination for the most part by the utilization of inhabiting restorative gadgets including (focal) venous and urinary catheters (Paganelli et al., 2013). Honey has been recommended as a powerful specialist to lessen biofilm arrangement by pathogenic microscopic organisms, for example, E. coli O157:H7 (Lee et al., 2011). Past investigation thought about the viability of Gelam Honey alongside Manuka Honey in the decrease of built up biofilm mass and restraint of biofilm arrangement created by E. faecium and E. faecalis. As per the outcomes, in spite of the fact that Manuka Honey was observed to be progressively better than Gelam Honey regarding diminishing the set up biofilm mass in the greater part of the bacterial strains, the impact was similar in both Honeys for their capacity to forestall the biofilm development. Generally speaking, this examination recommended the potential utilization of Gelam Honey as biofilm repressing specialist in the emergency clinic or other medicinal services offices to decrease the danger of pollution by an irresistible operator which, present unsafe impacts to patients (Ng et al., 2014).

Another investigation by (Aljadi et al., 2003) concentrated on the impact of phenolic concentrates got from Gelam and coconut Honey on E. coli and MSSA and MRSA strains. Results in the juices weakening measure showed that phenolic concentrate of Gelam Honey at 1.3 mg/mL focus somewhat hindered the development of every single bacterial strain, and all microscopic organisms were observed to be totally repressed at ≥1.95 mg/mL fixation. As opposed to these outcomes, phenolic concentrate of coconut Honey neglected to show the comparable impact at 1.3 mg/mL fixation. In any case, the concentrate halfway repressed the development of S. aureus and MSSA at 1.95 mg/mL focus, and complete hindrance of every single bacterial strain was shown at ≥2.6 mg/mL. Consequent investigation utilizing plate dissemination test demonstrated that Gelam Honey separate effectively hindered all tried bacterial strains in a portion subordinate way at the purpose of its most reduced (0.65 mg) to the most noteworthy (3.25 mg) focuses. They further proposed that these dissimilar antimicrobial properties of Gelam and coconut Honey were ascribed to the nearness of phenolic substance; Gelam Honey had higher phenolics (benzoic corrosive, gallic corrosive, cinnamic corrosive, caffeic corrosive, and ferulic corrosive) than that of coconut Honey extricate (benzoic corrosive, gallic corrosive, and caffeic corrosive). Along these lines, it isn’t amazing that the impacts are progressively articulated in Gelam Honey contrasted with coconut Honey (Aljadi et al., 2003).

Gelam honey as an anti-cancer
Basic treatment modalities for malignant growth
utilizing chemotherapy and radiotherapy in some cases represent an antagonistic impact on patients as they can be deadly to other feasible cells in the body (Ahmed et al., 2013). Along these lines, moving worldview toward the utilization of normal items as an elective treatment has pulled in a lot of research intrigue these years (Premratanachai et al., 2014). Honey is among the common item which is effectively investigated in numerous examinations for its anticancer properties. The components by which Honey applied its anticancer impacts are commonly through its capacity to prompt apoptosis through up-guideline of professional apoptotic proteins (p53, Bax, caspase 3, and caspase 9) and downregulation of hostile to apoptotic protein Bcl-2 other than restraining the proliferative limit of carcinogenic cells (Ahmed et al., 2013). Various past investigations have proposed that Gelam Honey have hostile to proliferative limit against malignancy cell lines. In 2011, Abu and partners tried the counter proliferative limit of Gelam Honey against a few human malignant growth cell lines (bosom adenocarcinoma, MCF-7; colorectal carcinoma, HCT116; alveolar basal epithelial adenocarcinoma, A549 and hepatocellular, HepG2). Results demonstrated that Gelam Honey applied its enemy of proliferative impact and instigate cell passing in all tried disease cell lines in a period and portion subordinate way when there was a noteworthy decrease in the development of HCT116 cell line at 24, 48, and 72 h with the IC50 estimations of 15.30, 4.31, and 3.98 % (v/v), individually. In this way, the most extreme cytotoxic impact was accomplished at 72 h at a centralization of 3.98% (v/v). Along these lines, Gelam Honey displayed most extreme cytotoxic impact against MCF-7 at 72 h with IC50 estimation of 6.31% (v/v), proposing its potential as a chemopreventive specialist against malignant growth (Abu et al., 2011).

Fig. 1. Honey Comb.

Besides, (Jubri et al., 2012) explored the counter proliferative impacts of Gelam Honey on liver malignant growth (HepG2) and typical liver (WRL-68) cell lines. It has been discovered that Gelam Honey showed hostile to proliferative limit against both cell lines in a portion subordinate way with the IC50 estimations of 25% and 70%, separately, for HepG2 and WRL-68 cells. Further examination utilizing bromodeoxyuridine test uncovered that Gelam Honey brought about the abatement in HepG2 cell expansion at 3–70% focuses. In addition, they found that HepG2 cells treated with Gelam Honey at IC50 portion of 25% after 48 h hatching showed cell shrinkage in this manner supporting the viability of Gelam Honey as an elective treatment against malignant growth.
Gelam Honey as the counter proliferative specialist through its capacity to instigate apoptosis (Jubri et al., 2012). In another investigation, (Fadhli et al., 2012) considered the counter proliferative impact of Gelam Honey on colon malignant growth (HCT116) cell line. Examination uncovered that Gelam Honey applied its suppressive impact on the cell multiplication in both time-and portion subordinate way with the IC\textsubscript{50} estimations of 2.1, 4.4, and 2.0%, separately, recorded at 24, 48, and 72 h.

In this manner, they presumed that Gelam Honey at IC\textsubscript{50} esteem at 2.0 % (v/v) focus for 72 h treatment was considered as viable to repress the multiplication of malignant cells, especially in the disease of colon. Notwithstanding that, they further theorized that the nearness of phenolic content at high fixation participated in encouraging malignant growth cell passings (Fadhli et al., 2012). Aside from that, a gathering of analysts from Universiti Kebangsaan Malaysia, Kuala Lumpur played out a relative investigation of the counter proliferative impacts of Gelam and Nenas Honey on colon malignant growth (HT29) cell line. They broke down the disease cells utilizing the 3-(4,5-dimethylthiazol-2-yl)- 5-(3-carboxymethoxyphenyl)- 2-(4-sulfophenyl)- 2H-tetrazolium (MTS) examine subsequent to hatching the cells with Gelam and Nenas Honey at different focuses from 0 to 150 mg/mL. Gelam Honey was exhibited to be more predominant than that of Nenas Honey in the concealment of colon malignant growth cell with the IC\textsubscript{50} estimations of 39.0 mg/mL and 85.5 mg/mL, individually. Results likewise demonstrated that colon malignant growth cells treated with Gelam Honey at its IC\textsubscript{50} focus prompted expanded all out DNA harm and level of apoptotic cells contrasted with control (Wen et al., 2012).

There is developing proof featuring the significance of joining explicit dietary phytochemicals which may give defensive preferred position against malignant growth contrasted with free mixes (de Kok. In this way, a few investigations took activities to play out a mix treatment of Gelam Honey alongside other characteristic sources to see whether they can act synergistically to hinder the development of malignant growth cells or not. Hakim played out an examination with the essential target to survey the viability of blend treatment between Gelam Honey and ginger concentrate in expanding the effect of 5-fluorouracil (5-FU) on colorectal malignant growth (HCT116) cell development restraint and apoptosis. 5-FU is a standout amongst the most much of the time utilized chemotherapeutic specialists to treat an expansive scope of malignancies including colorectal disease. The component by which this medication showed its anticancer impacts is through the hindrance of thymidylate synthase and fuse of its antimetabolites into RNA and DNA (Longley et al., 2003). As indicated by (Hakim et al., 2014), introductory treatment with ginger concentrate alone or Gelam Honey demonstrated a surprisingly unique enemy of proliferative limit between these two mixes. Ginger concentrate displayed an unrivaled enemy of proliferative limit against colorectal malignant growth cells with an IC\textsubscript{50} estimation of 3 mg/mL contrasted with Gelam Honey at 75 mg/mL. Resulting test by joining 2 mg/mL of ginger concentrate with Gelam Honey effectively repressed the development of malignancy cells with an IC50 estimation of Gelam Honey<30 mg/mL, lower than that of single treatment with Gelam Honey alone (75 mg/mL). Additionally, the mix file (CI) at 0.960 which is lower than 1 shows the synergism between these mixes. Aside from that, they found that cotreatment impact between ginger concentrate and Gelam Honey with 5-FU brought about huge decrease of cell development.
by 72%, 75%, and 80%, multiple times higher than the treatment with 5-FU alone, proposing that these mixes further upgrade the impact of 5-FU in stifling the development of disease cells. In the accompanying examination, it was discovered that Gelam Honey and ginger concentrate communicates with one another in a portion subordinate way at a mix portion of 32 mg/ml and 2 mg/mL, individually, to actuate the apoptotic movement of colorectal malignant growth cells. In this manner, they proposed that joined treatment with these normal mixes could build the chemotherapeutic impact of 5-FU against this malignancy (Hakim et al., 2014).

In spite of these promising outcomes, the flagging pathway systems engaged with the chemotherapeutic impact of Gelam Honey joined with ginger concentrate stays to be clarified. In this manner, a couple of studies have been attempted to unwind the counter malignant growth components required during the mix of these mixes. In a past investigation of (Tahir et al., 2005), the potential associations between unrefined ginger concentrate and Gelam Honey to repress the development of colorectal malignant growth (HT29) cell line have been researched. The investigations were led by treating colorectal malignant growth cells with an autonomous and blend treatment between ginger concentrate and Gelam Honey utilizing a scope of Honey focuses (1-70 mg/mL) and fixed groupings of ginger concentrate at 2, 3, or 4 mg/mL. Aftereffects of MTS measure had proposed the synergistic collaborations of the two mixes when the IC_{50} estimations of the blend medications between ginger concentrate (3 mg/mL) in addition to Gelam Honey (27 mg/mL) with a CI of <1 (CI = 1, >1, and < 1 signifies additivity, opposition, and synergism, separately) were observed to be lower than that of free treatment with ginger and Gelam Honey at 5.2 mg/mL and 80 mg/mL, individually. In addition, the two mixes have been appeared to work synergistically to actuate early apoptosis through an expansion in the statement of caspase 9 and IκB qualities pursued by under-articulation of KRAS, ERK, AKT, Bcl-xL, and NFXB (p65) qualities. In general, think about discoveries infer that amalgamation of ginger concentrate with Gelam Honey is very successful to upgrade the cytotoxic movement and subdue the
development of malignant growth cells by tweaking the KRAS/ERK/PI3K/AKT pathways, in this way, holds incredible potential to be utilized as a colorectal chemopreventive operator later on of (Tahir et al., 2005).

Another investigation made endeavors to investigate the synergistic impacts of Gelam Honey and ginger concentrate on colon malignancy (HCT116) cells through mTOR, Wnt/β-catenin and apoptosis flagging pathways (Wee et al., 2015). The mammalian focus of rapamycin (mTOR) and Wnt/β-catenin pathways is interconnected in the multistep procedures of colorectal carcinogenesis (Wang et al., 2014; Mashima et al., 2017). It was appeared by the outcomes that free treatment with Gelam Honey and ginger concentrate prompted the abatement in malignant growth cell feasibility in a portion subordinate way with the IC50 estimations of 88 mg/mL and 2.15 mg/mL, separately. Then again, consolidated treatment with 2 mg/mL ginger concentrate brought about the development hindrance of most malignancy cells with an IC50 estimation of Gelam Honey at 31 mg/mL, fundamentally lower than single treatment with Gelam Honey alone (88 mg/mL). Their works additionally demonstrated that joined treatment works synergistically to lessen the declaration of Akt, mTOR, Raptor, Rictor, β-catenin, Gsk3β, Tcf4, and cyclin D1 qualities while cytochrome C and caspase 3 qualities were up-managed. In this manner, they hypothesized that the methodology to consolidate both normal mixes holds incredible potential as chemo preventive operator against colorectal malignant growth through hindrance of these flagging pathways (Wee et al., 2015).

**Gelam honey as an anti-inflammatory**

Irritation is a body resistance component against disease, tissue pressure, and damage. It works by discharging different incendiary flag, for example, cytokines, chemokines, biogenic amines, and eicosanoids which result in huge number changes in different organic procedures running from vascular reactions to alterations of body temperature (Kotas et al., 2015). Plus, irritation likewise assumes a key job in the improvement of expansive range of complex infections including immune system sicknesses, metabolic disorder, neurodegenerative ailments, malignancies, and cardiovascular ailments (Murakami et al., 2012). The mitogen-initiated protein kinase (MAPK) and atomic factor kappa B (NF-κB) flagging pathways are among basic components in the incendiary reaction that is usually dysregulated in malignancies (Porcza et al., 2016). NF-κB flagging has been accounted for to assume a critical job in the guideline of tumor angiogenesis and obstrusiveness, furthermore, to give a defensive preferred position for disease cells to withstand apoptosis (Fan et al., 2013). Different examinations have been attempted by various gatherings of scientists to research the calming properties of Gelam Honey. In one investigation, Gelam Honey has been accounted for to lessen the actuation of NF-κB and MAPK in a portion subordinate way in pancreatic hamster (HIT-T15) cell line at groupings of 20, 40, 60, and 80 μg/mL for 24 h (Batumalaie et al., 2013). Another gathering of scientists found that HIT-T15 cell line treated with Gelam Honey at comparable focuses recently detailed by (Batumalaie et al., 2013) had brought about under-articulation of phosphorylated JNK, IKK-β, and IRS-1 other than diminished articulation of genius provocative cytokines, for example, tumor putrefaction factor alpha (TNF-α), interleukin (IL)- 6, and IL-1β (P < 0.05). Taken together, look into discoveries featured the potential utilization of Gelam Honey in controlling the aggravation instigated flagging pathways (Safi et al., 2010).

Kassim et al. (2010) utilized a creature model (male Sprague Dawley rodents) to survey the inhibitory movement of Gelam Honey and its methanolic and acetyl acetic acid derivation removes on nitric oxide (NO) and prostaglandin E2 (PGE2) in fiery tissues. In this examination, edema was prompted in the non-insusceptible provocative and nociceptive model by infusing the rodents' paw utilizing 1% g/mL carrageenan while the invulnerable fiery model was exposed to lipopolysaccharide (LPS) infusion to think
about the mitigating impacts of Gelam Honey. Their examination uncovered that Gelam Honey, just as its methanolic and ethyl acetic acid derivation, separates altogether decreased the edema (P < 0.05) and torment in fiery tissues other than showing an intense inhibitory exercises against NO and PGE2 in exudates of paw tissues in the two models (P < 0.05). Both NO and PGE2 are significant middle people of aggravation. In view of their exploration discoveries, Gelam Honey, and its concentrates have been appeared to lessen the incendiary movement by diminishing the primary fiery signs (restraint of swelling and agony decrease) and markers of irritation (NO and PGE2). They further detailed that the nearness of real phenolic mixes in the methanolic and acetyl acetic acid derivation concentrates including gallic corrosive, ellagic corrosive, caffeic corrosive, luteolin, chrysin, and quercetin added to the mitigating action of Gelam Honey(Kassim et al., 2010). Aside from that, led another examination to research the impact of Gelam Honey in irritation initiated rodents via carrageenan. Gelam Honey was found to lessen the arrangement of edema in time- and portion subordinate way when the treatment was directed at the centralization of 1 or 2 g/kg of body weight (P < 0.05) for 1–7 days. In light of their report, Gelam Honey displayed higher hindrance of edema at 54.23% and 59.86%, separately, when regulated with Gelam Honey at 1 or 2 g/kg of body weight in 7 days treatment contrasted with 26.58% and 29.11%, as saw on 1 day treatment utilizing the comparative dosages of Gelam Honey. Additionally, they found that oral organization of Gelam Honey at 1 or 2 g/kg of body weight let to a huge decrease in NO, PGE2, and IL-6 levels in plasma and under-articulation of provocative related catalysts (inducible nitric oxide synthase [iNOS] and cyclooxygenase [COX]-2), expert incendiary cytokines (TNF-α and IL-6) qualities and proteins in rodents’ paw tissues. Strikingly, the calming impact of Gelam Honey, especially at a portion of 2 g/kg of body weight was observed to be tantamount with that impact of nonsteroidal mitigating drug Indomethacin (10 mg/kg of body weight), recommending its potential as common calming specialist to be popularized soon. Late work from a similar gathering of analysts attempted to clarify the calming impact of Gelam Honey in carrageenan-initiated rodent paw aggravation through the NF-κB flagging pathway (Hussein et al., 2013). This investigation connected comparable dosages of Gelam Honey (1 or 2 g/kg of body weight) and treatment period as portrayed from their past examination. They found that expanded NF-κB (p65 and p50) and IkBα quality articulations in excited rodent paws because of carrageenan infusion were strikingly constricted (P < 0.05) by Gelam Honey in day 1 and day 7 models. They likewise announced that these impacts were progressively articulated in the treatment with 2 g/kg of body weight for 7 days, about like that impact of the treatment utilizing Indomethacin (10 mg/kg of body weight). In addition, they likewise centered on the declaration of COX-2 and TNF-α in this investigation. The two proteins are among the focal controllers of aggravation (Esposito et al., 2009; Chen et al., 2010). During aggravation, when the translation factor NF-κB was enacted, this outcomes in the up-guideline of expert incendiary middle person qualities articulations including IL-1β, IL-6, iNOS, COX-2, and TNF-α (Gosh et al., 1998). In this way, restraining NF-κB actuation and its translocation into the core other than decreasing the arrival of professional provocative arbiters have been the essential center nowadays to diminish irritation (Hussein et al., 2013). In view of the immunochemistry examinations, carrageenan-prompted irritation gathering had higher COX-2 articulation (80.6%) before treatment with Gelam Honey. Treatment with 2 g/kg of body weight with Gelam Honey for 7 days brought about a higher decrease of COX-2 articulation (26.29%) contrasted with day 1 (44.14%). Along these lines, rodents infused with carrageenan exhibited high TNF-α protein articulation (68.95%) before treatment with Gelam Honey. Their examination uncovered that aggravated rodent paws treated with 1 or 2 g/kg of body weight for 7 days prompted huge decrease in TNF-α protein articulation at 29.53% and 22.80%, individually, contrasted with day 1 treatment (53.75% and 30.11%). In general, they proposed that the
inhibitory component of Gelam Honey occurred through the inactivation of NF-κB, which thusly hinders the IκBα corruption and atomic translocation of NF-κB subunits, p65 and p50 in this way repress NF-κB authoritative to its objective DNA. Therefore, the transcriptional action of a few quantities of expert incendiary qualities including COX-2, TNF-α, IL-6, and iNOS were hindered (Hussein et al., 2013).

An autonomous investigation by (Kassim et al., 2012) assessed the calming impact of Gelam Honey utilizing rodents with LPS-prompted endotoxemia. LPS is the primary part of bacterial external layer found in Gram-negative microorganisms that fill in as a physical hindrance to give defensive favorable position for the microscopic organisms from the environment. It additionally assumes a critical job inside the safe framework as a marker to distinguish the intrusion of pathogenic microbes, advancement of provocative reaction and can possibly actuate cytotoxic stun (Rosenfeld et al., 2006). In this examination, endotoxemia prompted rodents got 60 mg/kg, 300 mg/kg, and 600 mg/kg portion of an answer containing Gelam Honey weakened in 1 mL saline while the control bunch just gotten 1 mL saline infused intravenously through the tail vein. Serum dimensions of TNF-α, IL-1, IL-6, IL-10, NO, and heme oxygenase-1 (HO-1) were inspected after 4 h treatment utilizing a protein connected immunosorbent measure (ELISA).

In light of the outcomes, Gelam Honey was accounted for to cause a critical decrease in the cytokine TNF-α, IL-1, IL-6, IL-10, and NO dimensions while expanding the cytokine TNF-α, IL-1, IL-6, IL-10, and NO dimensions while expanding the HO-1 level after 4 h treatment, in this way shielding rodents from endotoxemia. HO-1 has been appeared to improve survival in deadly endotoxemia in creature models.

Therefore, hindering the cytokines, NO, and high versatility bunch protein B1 discharge while invigorating the outflow of HO-1 in light of LPS fill in as a significant security procedure against endotoxemia (Tsoyi et al., 2009).

Periodontitis, characterized by gingival aggravation, periodontal pocket arrangement and the advancement of bacterial plaque which thusly lead to alveolar bone obliteration and tooth misfortune is among the major ceaseless fiery illnesses in grown-ups over the globe (Hamzah et al., 2014). Since there has been expanding enthusiasm toward the utilization of common items in the dentistry field, past work by Aziz searched for calming impacts of Gelam Honey in a periodontitis-initiated Sprague-Dawley rodent model. This investigation was led by reallocating the rodents into 4 particular gatherings; NLS (control treated with saline), NLH (control treated with Gelam Honey and 3 g/kg of body weight), LS (periodontitis treated with saline), and LH (periodontitis treated with Gelam Honey and 3 g/kg of body weight). Examination uncovered that Gelam Honey caused a huge decrease in IL-1β levels in periodontitis instigated rodents with an all-out decrease recorded at 21.26% and 81.27%, individually, in plasma and tissue tests when estimated by ELISA and immunohistochemical recoloring. Subsequently, the outcomes obviously featured the viability of Gelam Honey in lightening the expanded dimension of provocative middle person in periodontal illness (Aziz et al., 2014).

**Gelam honey as a wound healing**

Wound recuperating is a multi-step procedures comprising of three consecutive stages known as aggravation, multiplication, and development. Honey has long being connected in the treatment of twisted since the antiquated occasions (Molan et al., 2015). Rising proof from the clinical preliminaries has been supporting the adequacy of Honey to treat an assortment of intense and endless injuries. (Wijesinghe et al., 2009) played out a randomized controlled preliminary to look at the proficiency of Honey than different dressings, especially silver sulfadiazine (SSD)- impregnated bandage including 624 subjects from 8 free investigations. As per the outcome, they found that Honey was related with improved rate of recuperating (chances proportion, chances proportion 6.1, 95% certainty interim: 3.7–9.9) at 15 days, in this manner recommending its
prevalence thought about over different dressings (Wijesinghe et al., 2009). Another examination which planned to analyze the viability of Honey dressing than the ethoxy-aminoacidine in addition to nitrofurazone dressing found that patients who got Honey dressing had an amazingly better weight ulcer scale for mending scores than those treated with ethoxy-aminoacidine in addition to nitrofurazone dressing at 5-weeks (Günes et al., 2007).

The injury recuperating capability of Gelam Honey has been investigated by various past examinations. Aljady and teammates assessed the viability of Gelam Honey during the time spent injury recuperating by looking on the biophysical and biochemical changes in Sprague-Dawley rodent model. Wound mending limit of Gelam Honey was evaluated by following the injured regions onto a straightforward plastic network while figuring those zones with explicit checking recipe. They found that best oral and topical organization of Gelam Honey on recuperating would be at 1.5–2.0 mL and 0.1–0.15 mL/cm2 fixation, individually. Moreover, high DNA substance following Gelam Honey treatment estimated on day 4 (P < 0.05), days 8, 12, and 16 (P < 0.01) filled in as a pointer for expanded cell multiplication in the recently framed granulation tissue.

In addition, expanded collagen content on days 8 and 12 (P < 0.05) and day 16 (P < 0.01) after Honey treatment in the granulation tissue was conjured to be because of the nearness of elevated amounts of glycine, methionine, arginine, and proline that assume basic jobs in collagen development and testimony. Likewise, they revealed that expanded dimension of uronic corrosive on days 4, 8, and 12 (P < 0.01), and days 16 (P < 0.05), and hexosamine on days 4, 12, and 16 (P < 0.05), and day 8 (P < 0.01) contrasted with control was demonstrative of the amalgamation of glycosaminoglycans, the primary segments of extracellular grid to be incorporated during wound recuperating and go about as a format for the testimony of collagen and elastin. In addition, expanded level of wound constriction rate and serum egg whites levels were demonstrative of quickened wound mending given by Gelam Honey (Aljady et al., 2002).

Rigidity, portrayed as the breaking quality of a material separated by its cross-sectional territory is perceived as a perfect physiologic measure to assess an injury's capacity to oppose strain (Ireton et al., 2013). Also, it fills in as a significant parameter which demonstrates the subdermal association of the collagen filaments in the recently saved collagen (Jimenez et al., 1999). Rozaini et al. (2004) made a similar investigation to examine the elasticity of consume twisted mending in Sprague-Dawley rodents treated with Gelam and Nenas Honey. The rodents were given both Honeys at a portion of 0.5 mL multiple times once a day while the control gathering did not get any treatment. It has been discovered that Gelam Honey treated gathering displayed higher estimations of elasticity (MPa) at days 3 (0.93 versus 0.81), days 7 (1.55 versus 1.35), days 14 (1.71 versus 1.47), days 21 (2.47 versus 1.97), and days 28 (2.80 versus 2.08) post-damage than the control gathering.

In spite of the fact that Nenas Honey had higher rigidity esteems at days 3 (0.95 versus 0.81), days 14 (2.40 versus 1.47), days 21 (2.61 versus 1.97), and days 28 (3.95 versus 2.08) contrasted with control and Gelam Honey treated gatherings, the impact was equivalent in both Honeys as far as increasing the procedure of dermal injury mending (Rozaini et al., 2004). Resulting study embraced by comparative gathering of analysts to distinguish the injury recuperating properties of both Honeys on the histological premise found that Gelam Honey treated gathering had lower fiery cells, especially neutrophils on days 7 (26.50 versus 40.90), days 14 (6.86 versus 47.06), days 21 (3.93 versus 60.63), and days 28 (0.4 versus 51.43), and higher fibroblasts (44.56, 56.86, 68.26, 49.23, and 27.30, individually, on days 3, 7, 14, 21, and 28) and endothelial cells (5.76, 6.90, 6.56, 7.20, and 5.40, separately, on days 3, 7, 14, 21, and 28) contrasted with control gathering. By and large, they inferred that these outcomes were demonstrative of dynamic injury recuperating procedure given by Gelam Honey (Rozaini et al., 2004).
In the next year, these scientists led another investigation to assess the plainly visible changes of consume twisted recuperating in light of the treatment with different kinds of Honey (Gelam, coconut, Nenas, Manuka, and Durian). Information demonstrated that Gelam Honey had a higher level of wound withdrawal, estimated longitudinally post-consumed in days 7 (5.60 versus 1.30), days 14 (33.10 versus 6.75), days 21 (56.10 versus 19.41), and days 28 (83.86 versus 46.48) contrasted with control. Manuka Honey additionally showed a comparable impact, when the level of wound withdrawal was recorded at 6.05, 32.86, 52.66, and 87.20, separately, on comparable treatment periods. In addition, the level of wound withdrawal when estimated transversely in Gelam Honey treated gathering demonstrated a movement in a period subordinate way, with the most elevated esteem recorded at days 28 post-consumed (87.50 versus 50.21) contrasted with control. In addition, Manuka Honey likewise demonstrated most astounding level of twisted withdrawal at days 28 (90.71 versus 50.21) contrasted with control and Gelam Honey treated gathering, in this way, recommending topical use of Manuka and Gelam Honeys are profoundly compelling to quicken the injury recuperating Gelam Honey consolidation into the hydrogel as twisted dressing with high mending capacity than the popularized SSD-cream treated injury (Yusof et al., 2007).

Other examination explored the injury recuperating adequacy of Gelam Honey by fusin 6% (v/v) Gelam Honey into the hydrogel dressing comprised of 15% (w/v) PVP, 1% (w/v) protein free agar arrangement, and 1% (v/v) PEG. They found that Gelam Honey based hydrogel dressing expanded the rate of consume twisted mending as seen by a higher decrease in twisted size at 81.78% and 91.27%, separately, following 21 and 28 days post-consume (P < 0.05). The tiny examination had shown a huge movement in dermal fix other than higher re-epithelialization process in the injured territory treated with Gelam Honey when contrasted with different gatherings. Moreover, they likewise announced a huge decrease in the incendiary reaction in Gelam Honey treated gathering at days 7 post-consumed (P < 0.05). In addition, atomic examination uncovered that treatment with Gelam Honey at the injured region brought about critical decreases in the statement of master incendiary cytokines (IL-1α, IL-1β, and IL-6) engaged with twisted mending, as higher articulation of these ace provocative go betweens in consume wounds may disable the injury recuperating process (Mohd et al., 2012). The viability of Gelam Honey as a strong specialist of wound mending was additionally investigated by another gathering of scientists from the University of Malaya, Kuala Lumpur in male grown-up Sprague-Dawley rodents. The rodents were allocated into four unique gatherings; the untreated control gathering did not get any treatment, positive control gathering got intrasite gel comprised of a blend of changed carboxymethyl cellulose polymer, propylene glycol and water, and negative control gathering was given topical treatment with typical saline while the exploratory gathering got the topical treatment with Gelam Honey. Results demonstrated that Gelam Honey treated gathering had lower mending time (mean 13.17 days versus 16.67 days versus 15.83 days) contrasted with untreated and saline gatherings, separately. The mending time additionally was observed to be practically identical with the impact of intrasite gel that fills in as positive control (mean 13.17 and 13 days, separately). Naturally visible and histological evaluation demonstrated that Gelam Honey quickened and histological appraisal demonstrated that Gelam Honey quickened the procedure of wound recuperating contrasted with different gatherings. This impact was said to be ascribed to the nearness of H₂O₂, notwithstanding its healthful properties that presents fitting natural conditions to advance the mending procedure. The level of twisted constriction in Gelam Honey treated gathering notwithstanding the gathering that gets treatment with intrasite gel was additionally observed to be higher than the untreated and saline gatherings, further backings its potential as regular injury recuperating operator (Tan et al., 2012).
Conclusions
The research related to the Gelam honey has showed the positive impact on the treating the various sorts of diseases, their prevention and as the controlling factor. The useful effects of the Gelam honey leads to the betterment of the society and for their healthy and beneficial purposes. The demand of Gelam honey are increasing in the market day by day because of extensive research are doing on the biological activities of the Gelam honey.

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