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Review

The relevance of folkloric usage of plant galls as medicines: Finding the scientific rationale

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ABSTRACT

Galls, the abnormal growths in plants, induced by virus, bacteria, fungi, nematodes, arthropods, or even other plants, are akin to cancers in fauna. The galls which occur in a myriad of forms are phytochemically-distinct from the normal plant tissues, for these are the sites of tug-of-war, just like the granuloma in animals. To counter the stressors, in the form of the effector proteins of the invaders, the host plants elaborate a large repertoire of metabolites, which they normally will not produce. Perturbation of the jasmonic acid pathway, and the over-expression of auxin, and cytokinin, promote the tissue proliferation and the resultant galls. Though the plant family characteristics and the attackers determine the gall biochemistry, most of the galls are rich in bioactive phytochemicals such as phenolic acids, anthocyanins, purpurogallin, flavonoids, tannins, steroids, triterpenes, alkaloids, lipophilic components (tanshinone) etc. Throughout the long trajectory of evolution, humans have learned to use the galls as therapeutics, much like other plant parts. In diverse cultures, the evidence of folkloric usage of galls abound. Among others, galls from the plant genus like *Rhus*, *Pistacia*, *Quercus*, *Terminalia* etc. are popular as ethnomedicine. This review mines the literature on galling agents, and the medicinal relevance of galls.

1. Introduction

Galls or cecidia are abnormal growths in plants, which are akin to tumors in animals. In that way, galls are the cancer equivalent of humans and other animals. Considering the hazardous effect of galls on plants, there is a discipline of botany known as 'cecidology', the study of plant galls [1]. Almost all plants are prone to galling by microbes, nematodes, and arthropods. Invertebrates as arthropods and mollusks carry a myriad of microbes which can infect plants, following the mechanical damage to the tissues. Rice green leafhopper (*Nephotettix nigropictus*)-transmitted virus can destroy the rice plants. A number of virus (rice gall dwarf), bacteria (*Agrobacterium tumefaciens*, *Pseudomonas savastanoi*) [2], fungi (*Puccinia*, *Exobasidium*, *Ustilago*, *Pythium*, *Phytophthora*, *Hyaloperonospora*, *Albugo*, *Taphrina* etc.) [3], and nematodes (*Meloidogyne* spp.) have been identified, which induce plant galls. Also, the insects (wasps, midges, flies, aphids, mites, scale insects, psyllids, phylloxerans etc.) create gall by depositing their eggs on the plant parts. The emerged larvae feed on the plant parts, causing the gall formation. Galling by the arthropods induce the host plant to secrete a range of phytochemicals, which in normal condition, the plant would not generate, because the metabolic re-routing comes at a cost. These secondary metabolites are supposed to fight the invaders. The galling agents interfere with auxin- and cytokinin-elaboration pathways of the plants.

The Fig. 1 shows mite (*Aceria aloinis*)-caused galls in aloe (*Aloe* sp.). In fact, the parasitic plants like mistletoes, and the mushrooms also create galls on host trees. The Fig. 1 shows mistletoe (*Viscum* sp.)-caused galls on a sycamore (*Platanus* sp.) tree. Some variations of galls include crown gall, flower gall, leaf gall, stipule gall, pod gall, shoot gall etc. Oak (*Quercus* sp.), sycamore, ash (*Fraxinus* sp.), honey locust (*Gleditsia* sp.), elm (*Ulmus* sp.), willow (*Salix* sp.), pongam oil tree (*Millettia pinnata*), witch hazel (*Hamamelis* sp.), azalea (Rhododendron sp.), aloe, kalanchoë (Kalanchoe sp.), and peach (*Prunus persica*) are some common plants prone to galling. The syconia of fig (*Ficus* spp.) can have gall, caused by fig wasps (Superfamily Chalcidoidea, Family Agaonidae) [4]. However, almost all plants are affected by galling agents. A detailed list of galling agents and the affected plants have been listed in Table 1. The plants can tackle moderate galling, but heavy infestation can hamper plant vigor, and can lead to poor photosynthesis, leaf dropping, with eventual plant death. Gall-inducing

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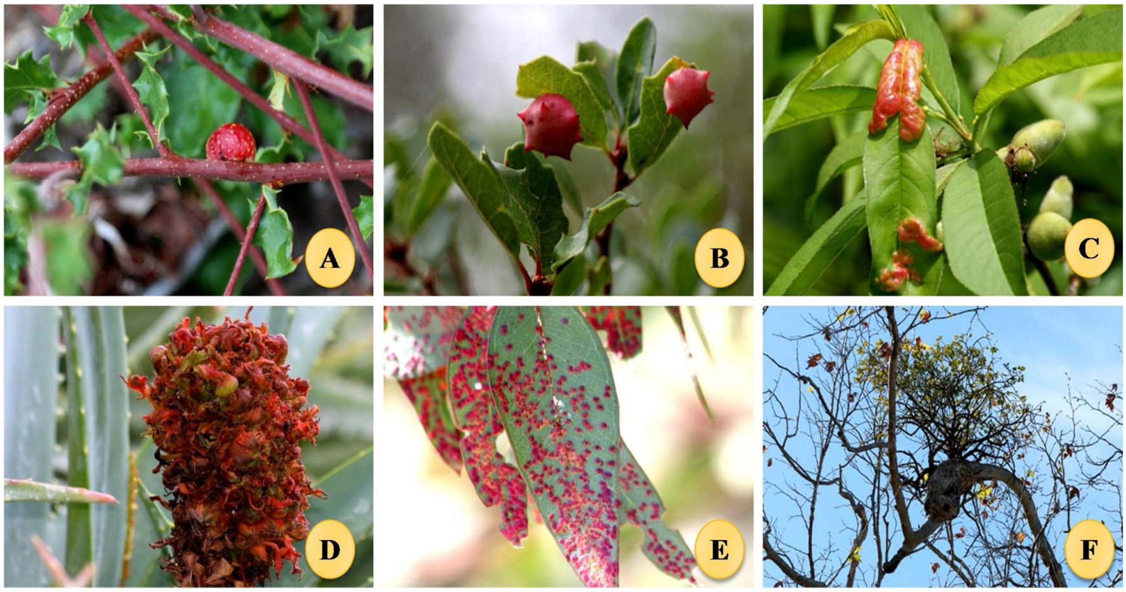

Fig. 1. Galls in different plants (A) oak (B) oak (C) peach (D) aloe (E) eucalyptus (F) mistletoe. The oak galls are reddish due to the anthocyanin pigments. Peach leaf curl is induced by *Taphrina deformans*, during the Spring season. Mite caused-gall in aloe is akin to cancer, with functional and structural features of the plant lost to the attacker's hijacking of signaling pathways. Psyllid-caused red bumps on the lower side of eucalyptus leaves affect the plant photosynthesis ability, and infect other plants. Where the haustorium of the parasite mistletoe penetrates the host plant tissue, a woody growth occurs.

arthropods and nematodes comprise some of the most devastating pests of global agricultural practice. Some examples of specific galling agent-host plant interactions include phylloxera (*Daktulosphaira vitifolia*) – grape (*Vitis vinifera*), the Hessian fly (*Mayetiola destructor*) – wheat (*Tritcum aestivum*), the Asian rice gall midge (*Orseolia oryzae*) – rice (*Oryza sativa*), the blue gum chalcid wasp (*Leptocybe invasa*) – *Eucalyptus* sp., as well as root-knot nematodes (*Meloidogyne* sp.) – tomato (*Lycopersicon esculentum*), among numerous other examples [5]. Gall-inducing insects have co-evolved with their host plants, and the nexus is largely parasitic, and complex. In some cases, the galling is infectious and the affected tree requires to be removed. However, some deviations have been observed where the host plants are benefitted by the galling. A gall wasp *Leptocybe invasa* invades river red gum (*Eucalyptus camaldulensis*). In this case, the infected plant appears to tackle cold stress better than the uninfected plants [6]. The higher frost resistance is explained to be due to the hyper-activated defense system [6]. It appears to be a situation like human autoimmunity, where the alert immune system suspects everything as a stressor, and escalates immune response. Also, some galls are commensal or symbiotic, such as the root nodules in legumes, caused by nitrogen-fixing bacteria *Rhizobium*.

The phytochemicals of galls are different than that of regular plant parts. The richness of secondary metabolites has led to the name 'physiologic sinks' for some galls. In fact, these pooled compounds in galls have attracted the attention of, and the exploitation by humans, since ages. Folkloric and pharmacopeia testify their uses in Chinese, Greek, and Indian folk remedies, among other cultures. The plant galls are used as household ingredients and medicines. The usage of galls from oaks as dyes, is an old practice [7]. Also, tanning, and ink making have been other uses of the galls. Gall-harbored larvae are consumed by some tribal communities. Plentiful ethnobotanical studies have reported the usage of galls for diverse illness alleviation. Common plant galls with therapeutic applications include *Rhus*, *Pistacia*, *Quercus*, *Terminalia* etc. Most of the galls are irregular, club-like, globose, chili, coral, cauliflower, curved, but some of them take the appearance of fruits, so wrongfully they are called 'apples'. Anatomical study of Chilean pepper tree (*Schinus polygamous*) plant galls showed tissue hyperplasia, dense trichomes, and large nymphal chambers [8]. This review discusses the published literature on plant galls with relevance to human healthcare, and proposes hypotheses that can be useful to the research community.

2. Gall phytochemistry

As mentioned before, the biochemical profiles of the galls are starkly different from the normal plant tissues. The aphid phylloxera abnormally induces stomata on the upper surface of grape leaves, which facilitate nutrient acquisition by the insect [9]. Also, the leaf transcription pathways for sucrose mobilization and glycolysis are altered [9]. Scientific investigations on the gall extracts have identified the bioactive components, explaining the underlying biological mechanisms. The phytochemicals in the galls include triterpene, gallic acid, ethyl gallate, catechin, epicatechin, tannic acid, resin, among a gamut of other components. Gall tissues encounter higher oxidative stress than the normal plant tissues. The elaboration of higher polyphenols, anthocyanins, flavonoids, and tannins are attributed as the effort to address the oxidative stresses [10]. The reddish appearance of some galls is likely to be due to the anthocyanins (Fig. 1). The red hues indicate the down-regulation in chlorophyll synthesis and the up-regulation of anthocyanin synthesis [11]. Higher anthocyanin production has been linked to the protection from stressors such as cold, nutrient deficiency, herbivory, and intense sunlight [12]. The galls triggered by the aphid *Slavum wertheimae* on wild pistachio trees revealed high quantity of terpenes, which was proposed as a defense strategy by the aphid to escape predation by herbivores [13]. All the current evidence indicates that galling cecidomyiid *Bruggmanniella* sp. insects transform the photo-assimilative abilities of the leaves in the Lauraceae family plants *Litsea acuminata* and *Machilus thunbergii*, into gall sinks [10]. The galling reduces the carotenoids and chlorophyll-related compounds, but increases total soluble sugar and free amino acids [10]. Purpurogallin, an antioxidative plant phenol, with immense biological attributes, has been detected in some galls [14,15]. This phenol showed antibacterial activity against methicillin-resistant *Staphylococcus aureus* (MRSA) [16], and inhibited the phosphopeptide binding domain of polo-like kinase 1 (Plk1) [17]. The chemical reaction between purpurogallin derivatives and nitrosobenzenes yields tetracyclic indenoquinolines, which possesses antiproliferative properties [18]. Further, purpurogallin could attenuate both proinflammatory cytokines (IL-6 and TNF-α) and late-onset inflammasome in subarachnoid hemorrhage-induced