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Invited Review Article

Phytochemistry and ethnomedicinal use of *Bergenia* species- A miraculous herb

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Abstract

The *Bergenia* species are used in folklore system of medicine and are instrumental in dissolving kidney and urinary bladder stones. This article aims to collate and analyse the available information on the ethnomedicinal and phytochemistry of *Bergenia* species found in India. A total of 104 ailments treated by *B. ciliata* were recorded besides being accredited with analgesic, antiviral, anti-inflammatory and antimalarial properties. *B. ligulate* is administered during dysentery due to its absorbent nature. The root and honey mixture are scoured down to enhance milk teeth growth. In the Indo-China locale; the leaves are grounded in a mortar, and the juice utilized for ear infections. Hot water concentrate of an entire dried plant of *B. ligulata* has been utilized orally for renal or urinary calculi. For the expulsion of round worms from the body, a portion of around 10 g of juice of rhizome paste of *B. ligulata* b.i.d. along with molasses are given for 3-4 days. The herb's rhizome was given either in powdered form or oral form to combat digestive, carminative, and stomach pain issues. The extraction from the root of *B. ligulata* with various organic solvents (petroleum ether, diethyl ether, chloroform, acetone, and ethanol) showed the presence of alkaloids, carbohydrates, flavonoids, glycosides, saponins, steroids, tannins and terpenoids in addition to bergenin. Due to presence of polyphenols *Bergenia* sp. can potentially be used in medicine and pharmacology.

Key words: *Bergenia* sp., Ethnopharmacology, Food system

Highlights

- The use of *Bergenia* species for treating ailments in traditional folk medicines dates a long time back.
- Primary endeavor to assemble most extreme divided writing about the ethnopharmacology and phytochemistry of the three *Bergenia* species.
- *Bergenia* species found in India can conceivably be utilized in the worldwide business and moving food enterprises as a flavoring, seasoning additive and natural preservative agent.

Introduction

Plants have played a vital role in maintaining human health since a long time, being an essential ingredient in daily essentials such as medicines, cosmetics, dyes, beverages, etc., thus actively contributing towards the improvement of human life. Nowadays, there has been a focus in every corner of the globe on plant research. Plants have always been known as efficient factories that are able to biosynthesize various chemically diverse, naturally available molecules. Utilization of herbal agents for treating an array of diseases including gastrointestinal, cardiovascular, metabolic disorders, etc. have surfaced up. The unavailability of modern drugs in rural India has led to its usage being 25%. The rest of the population dependence rests on herbal drugs for the treating their diseases (Gurav and Gurav, 2014). The ethnobotanical and ethnopharmacological studies have attracted investigators throughout the world.

Limited mostly to herbs and shrubs, the family Saxifragaceae boasts itself of having 80 genera and 1250 species worldwide. The typical

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character seen is that the bunch of blossom in the herb is not immediately supported by the basal whorl, but rests well above. The fruit is in a form of capsule with infinitesimal seeds. Many of its members grow in rocky places (Ruby *et al*., 2012). Economically, the three genera *Saxifrage*, *Heuchera*, and *Bergenia* are important most under the family Saxifragaceae. A group of about ten different species of flowering plants are referred to as *Bergenia* under family Saxifragaceae. These evergreen perennials are genuinely a variety that fills the shady or dappled spots in the garden beautifully where other plants tend to shy away. Being native to central Asia and hardy in nature, *Bergenia* does well in poor soil and harsh weather conditions, mainly found in Afghanistan, China, the Himalayas, and Mongolia,(https://www.homestratosphere.com/types-of-bergenia-flowers/). Flora of British India (Hooker, 1888) specifies three species of *Bergenia* reported from India. Similar reporting was found in The Wealth of India (Wehmer, 1948). India is blessed with three of its species, namely, *Bergenia ligulata*, *Bergenia ciliata* and *Bergenia stracheyi* (Fig. 1). The organically trademark highlights of the genus *Bergenia* include height within 50 cm, tender, rhizomes with leaf bases, white, pink or purple blossoms and year-round growth (Kumar and Tyagi, 2013a); and a conical capsule having minute seeds is the fruit**.** Various pieces of literature indicates that the genus *Bergenia* is having a wide range of applications towards a human civilization which are thoroughly studied and focused here.

Ethno-medicinal uses

The use of *Bergenia* species for treating ailments in traditional folk medicines dates a long time back. The Unani and Ayurveda system of medicine mention the use of rhizomes and roots as a bitter, astringent, laxative, abortifacient, tonic, used in the treatment of an explosive number of treatments including tumours, urinary discharge, heart diseases, piles, spleen enlargement, ulcers, dysuria, disease of bladders, pulmonary infection, dysentery, menorrhagia, diseases of lungs and liver, fever, and cough (Manjunatha, 2010; Alok *et al*., 2013). If the rhizomes are applied as a paste over the burn wounds for 3-4 days, it provides a soothing relief without leaving a scar. The same paste has been found to be used in setting of broken bones or in treatment of diarrhoea and fever when administered along with honey. Roots of *Bergenia* were useful to combat venereal diseases (Kumar and Tyagi, 2013a).

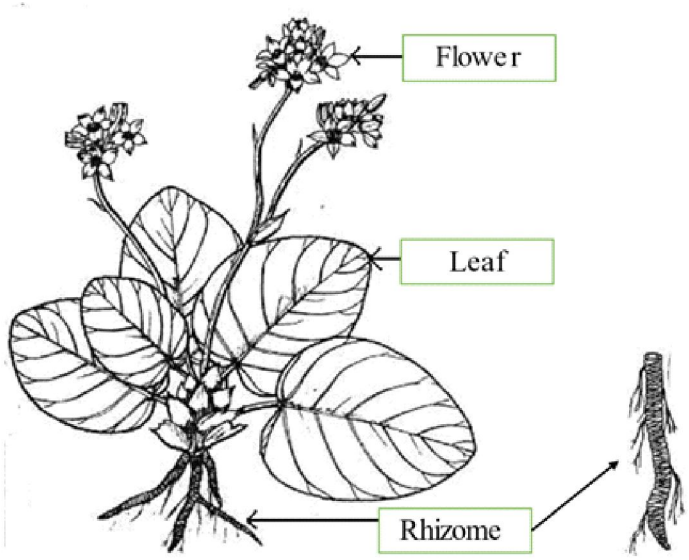

Fig. 1. Diagram of different parts of *Berginia ciliata*

Bergenia ligulata and its ethno-medicinal uses

The plant *B. ligulata* grows between rocks appearing to break them, which is otherwise called lithotriptic property. The ethnomedicinal writing teaches that in Ayurvedic and Unani medicinal cult, the underlying foundations of *B. ligulata* have cooling, purgative, pain relieving, abortifacient qualities and is utilized during treatment of calculi formed in vesicles, urinary releases, unnecessary uterus discharge, menorrhagia, illnesses of the urinary bladder, loose bowels, splenic growth, and heart infections (Kirtikar and Basu, 2005). It is administered during dysentery due to its absorbent nature. In Pakistan, the root and honey mixture are scoured down to enhance milk teeth growth in youngsters. In the Indo-China locale; the leaves are grounded in a mortar, and the juice utilized for ear infections (Chowdhary *et al*., 2009). Hot water concentrate of an entire dried plant of *B. ligulata* has been utilized orally for renal or urinary calculi (Sharma *et al*., 2017). For the expulsion of round worms from the body, grownups were allotted a portion of around 10 g of juice or rhizome paste of *B. ligulata* b.i.d. along with molasses for 3-4 days, furthermore for the treatment of cold in Nepal (Manandhar, 1995a; Bhattarai *et al*., 2006). In India, dried roots of *B. ligulata* accounted for treating wounds, cuts, boils and burns; its oral mixture for the treatment of diarrhoea, while its rootstock has additionally been utilized as masticator by grown-ups (Shah and Jain, 1988). A decoction of new roots of *B. ligulata* is taken orally by adults to treat urinary issues, stomach issues and urogenital affliction (Chandra and Pandey, 1983; Jain and Puri, 1984). The use of hot water concentrate applied remotely for boils and topical utilization for the treatment of ophthalmia have additionally been referenced (Gurav and Gurav, 2014).

Bergenia ciliata and its ethno-medicinal uses

Ahmad *et al*. (2018), when altogether examined the complete use *B. ciliata*, discovered that a sum of 104 afflictions were dealt, going from gastrointestinal, skin infections, renal/urinary problems, to gynaecological issues, ENT (Ear Nose Throat), fever, and even cancer when utilizing it. They further classified that the herb had found its use in treating gastrointestinal, skin diseases and urinary/renal diseases to be in the top three applications. The Himalayan realm has a deep-rooted history of the *Bergenia* rhizome being utilized in treating broken bones, fresh cuts, wounds, looseness of the bowels, and aspiratory contaminations by the locales (Rai *et al*., 2000; Pradhan and Badola, 2008). Traditional healers and locals in the state of Sikkim and the areas under Darjeeling district of West Bengal have been using rhizome of *B. ciliata* in the form of juice as an anti-tussive agent (Khan and Kumar, 2016). It was also used for the treatment of heart disease, haemorrhoids, stomach disorders and ophthalmia (Walter *et al*., 2013). Manandhar (1995b) revealed that in Nepal, rhizomes of *B. ciliata* had been taken by grown-ups as an antihelmintic. Roots and leaves of *B. ciliata* were also used in the treatment of blood cancer in Manipur, India (Imotomba and Devi, 2011). The extracts held high hopes and has got the potential towards the development of drugs that might be used to target tumours and to further check neoplastic growth and malignancy (Rajkumar *et al*., 2011). Bhattarai (1993) has reported that boiled juice of crushed rhizome of *B. ciliata* in water was effective for the treatment of chronic dysentery. Its decoction was likewise referenced to be taken orally by the human adults, as an antipyretic (Khan and Kumar, 2016). Though having a variety of modes of utilization or preparations, the most commonly used practice was powder, followed by decoction, liquid, paste, tea and extract (Ahmad *et al*., 2018).

Bergenia stracheyi and its ethno-medicinal uses

The presence of Bergenin in *Bergenia stracheyi* proved that this drug can be used to

treat arthritis in mice (Nazir *et al*., 2007). Interestingly, "Bragen", syrup used by the Zemithang Monpa people, is used for treating rheumatic pains in Arunachal Pradesh. One bray of washed, clear fresh leaves of *B. stracheyi* were crushed to prepare paste and mixed with 1/4 bray local millets wine to prepare the syrup (Chakraborty *et al*., 2017). In Kulu district of Himachal Pradesh, the powdered root are boiled in water and taken empty stomach, early in the morning to combat dysentery with stools having blood (Natarajan *et al*., 2000). Khan *et al*. (2015) investigated the traditional veterinary phytomedicines used and found out that the *B. stracheyi* sampled from an altitude of 4000-4500 m was used in treatment of headache, blood pressure, vomiting, arthritis, backache, delivery wounds, diarrhea and dysentery. Ballabh *et al*. (2008) reported its use in treating kidney and urinary disorders. In Kashmir, the herb's rhizome was given either in powdered form or Oral form to combat digestive, carminative, and stomach pain issues (Ijaz *et al*., 2020).

Phytochemistry

Nature is a rich wellspring of exceptionally assorted and imaginative synthetic constructions (Nazir *et al*., 2011). The relationship existing among people and plants is just about as old as mankind, tracing all the way back to the beginning of human progress. People have depended on plants for dress, food, fuel, sanctuary, and medication (Ruby *et al*., 2012). The day starting with a taste of natural tea, an unrefined concentrate, a phytopharmaceutical or home-grown combination or isolated compounds, can be ordered as the restorative utilization of plant (Aremu, 2009). The instrument for quality appraisal is the phytochemical assessment that incorporates chemo profiling, phytochemical screening, and marker compound examination (Bagul *et al*., 2003).

Metabolites are fundamental for the plant's development, improvement explicit capacity like pollinator fascination or guard against being eaten. Metabolites are of two kinds, first is essential or primary metabolites, and the subsequent one is auxiliary or secondary metabolites (Chauhan *et al*., 2013). Essential metabolites establish distinctive natural mixtures, like starches, lipids, proteins, and nucleic acids. They are found in the plants since they are the results of principal metabolic pathways, for example, the Krebs cycle, Glycolysis and Calvin cycle. Auxiliary metabolites are vital, as it discovers its use in people. Most drugs depend on plant substance designs and auxiliary metabolites. Auxiliary metabolites have been segregated from plants which give pharmacological impacts in people so that it is utilized as prescribed medicines. Some of the auxiliary or secondary metabolites which are therapeutically significant are given in table 1.

The essential phenolic compound 'bergenin' is the major component of *Bergenia* species (almost 0.9%) and other phenolic compounds are present in minor sum (Gurav and Gurav, 2014). The incorporated phenolic compounds include (+)- afzelechin, leucocyanidin, gallic acid, tannic acid, methyl gallate, (+)- catechin, (+)- catechin - 7-O-ß-D-glucopyranoside, 11-Ogalloyl bergenin; Paashaanolactone (Tucci *et al*., 1969; Dixit and Srivastava, 1989; Chandrareddy *et al*., 1998). It additionally contains sterols, tannin, mucilage and wax.

Phytochemistry of *Bergenia ligulata*

Rhizomes of *B. ligulata* showed a presence of various compound elements like; Coumarins: bergenin, 11-O-galloyl bergenin, 11-O-P-hydroxy benzoyl bergenin; 11-O-broto-catechuoyl bergenin, 4-0-galloyl bergenin; Flavonoids: (+) afzelechin, avicularin, catechin, eriodictyol-7-O-β-D glucopyranoside, reynoutrin; Benzenoids: arbutin, 6-O-P-hydroxy-benzoyl arbutin, 6-O-protocatechuoyl arbutin; 4-hydroxy benzoic acid; and Idehcxan-5-olide, 3-(6'- O-P-hydroxy) (Chandrareddy *et al*., 1998; Fuji *et al*., 1996). Coumarin (bergenin), tannic acid, gallic acid, minerals and

Table 1. Some important secondary metabolites found in *Bergenia* species of India and their activity (Chauhan *et al.*, 2013)

Secondary metabolites	Class of compound	Chemical formula	Major source	Activity
Bergenin	Phenol	$C_{14}H_{16}O_9$	*B. ligulata*, *B. ciliata*, *B. stracheyi*	Antioxidant, antimicrobial, countering arrythmia, anarchic effect
Tannic acid	Phenol	$C_{76}H_{52}O_{46}$	*B. ligulata*	Pharmaceutical applications
Gallic acid	Phenol	$C_7H_6O_5$	*B. ligulata*, *B. ciliata*	Antifungal, Antiviral, Cytotoxicity, Antioxidant
Stigmasterol	Sterol	$C_{29}H_{48}O$	*B. ligulata*	Precursor of vit. D_3, antioxidant, hypoglycemic
β-Sitosterol	Sterol	$C_{29}H_{50}O$	*B. ligulata*	Cholestrol inhibition, treating prostatic hyperplasia and carcinoma.
Catechin	Phenol	$C_{15}H_{14}O_6$	*B. ciliata*	Histidine decarboxylase inhibitor
(+)-Afzelechin	Flavonoid	$C_{15}H_{14}O_5$	*B. ligulata*	α-glucosidase inhibitor activity
1,8-cineole	Terpenoid	$C_{10}H_{18}O$	*B. ligulata*	Control cytokine production, perfumery, rhinosinusitis treatment
Isovaleric acid	Fatty acid	$C_5H_{10}O_2$	*B. ligulata*	Anticonvulsant agent, perfumery
Arbutin	Glycoside	$C_{12}H_{16}O_7$	*B. ciliata*	Melanin lightening
Phytol	Diterpene alcohol	$C_{20}H_{40}O$	*B. stracheyi*	Precursor of synthetic vit. E and vit.K
Caryophyllene	Terpene	$C_{15}H_{24}$	*B .stracheyi*	dietary cannabinoid
Damascenone	Terpene	$C_{13}H_{18}O$	*B. stracheyi*	Perfumery
β-eudesmol	Terpenoid	$C_{15}H_{26}O$	*B. stracheyi*	Inhibits platelet aggregation, hypotensive
3-methyl-2-buten-1-ol	Alcohol	$C_5H_{10}O$	*B. stracheyi*	Perfumery
(Z)-asarone	Phenol	$C_{12}H_{16}O_3$	*B. ligulata*	Treat neuro-inflammotary diseases
Terpinen-4-ol	Alcohol	$C_{10}H_{18}O$	*B. ligulata*	Anti-inflammatory, antioxidative, anti-tumour

wax was found in the seeds of *B. ligulata* (Singh *et al.*, 2009). The extraction from the root of *B. ligulata* with various organic solvents (petroleum ether, diethyl ether, chloroform, acetone, and ethanol) was carried out in increasing order of polarity. The preliminary investigation showed the presence of alkaloids, carbohydrates, flavonoids, glycosides, saponins, steroids, tannins and terpenoids (Ruby *et al.*, 2012). The thin layer and column chromatography of diethyl ether and acetone extract isolated β-sitosterol, stigmasterol, tannic acid and gallic acid. To establish the chemical structure of the isolated compounds, noble techniques like Ultraviolet (UV), Infrared (IR) and Nuclear Magnetic Resonance (NMR) spectroscopy were used. Thin Layer Chromatography (TLC) again confirmed this with the standard sample (Reddy *et al.*, 1999). Polyphenols were the mainly focused active ingredient, among which bergenin is studied and applied frequently. Thus, the plant of

Bergenia can be used in medicine (Singh *et al*., 2007).

Phytochemistry of *Bergenia ciliata*

A study on *B. ciliata,* when screened for its phytochemical constitution, enlighted all, the existence of terpenoids, tannins, flavonoids, saponins, and steroids (Uddin *et al*., 2012). Presence of alkaloids, tannins, flavonoids, coumarins and glycosides in *B. ciliata* rhizome was accounted by González-Castejón and Rodriguez-Casado (2011). In writing, Chauhan *et al*. (2012) inspected the presence of numerous secondary metabolites in the genus *Bergenia*. Ahmad *et al*. (2018) reported 11 significant classes of phytochemicals in *B. ciliata*. Gyawali and Kim (2012) announced the occurrence of 43 volatile natural mixtures seven belonging to chemical classes of acid, thirteen of alcohol, five of aldehyde, four of ester, three of hydrocarbon, eight of ketone, two of N-containing compounds and one for miscellaneous in *B. ciliata*. From the ethereal part of the leaves, hydroquinones (benzoids) were secluded. From the rhizome part, uniquely disengaged compounds are (+)-afzelechin, quercetin-3-o-β-d-glucopyranoside, arbutin, hydroxy benzyl arbutin, bergenin, 4-O-galloybergenin, p-hydroxybenzoic acid, protocatechuic acid, 6-O-protocatechuoylarbutin, 11-O-hydroxy-benzylbergenin and 6-O-p-hydroxy benzyl parasorboside (Fuji *et al*., 1996). *B. ciliata* contains several significant phytochemicals such as bergenin, gallic acid, (+) – catechin, paashanolactone, sitoindoside, quercetin, and (+) afzelechin (Dharmender *et al*., 2010). Not taking the alcohol strengths into account, the chemical compounds steroid, triterpenoid, flavonoid, tannins, carbohydrates and saponins were the composition of tinctures (Panda, 2002). The rhizome of *B.ciliata*, yielded gallolyted leucoanthocyanidin-4-(2-galloyl) glucoside as well (Yadav *et al*., 2011).

Phytochemistry of *Bergenia stracheyi*

Portrayal of flavonoids from antioxidant guided fractionation of aqueous (aq.) alcoholic concentraton derived from the flowers and leaves of *B. stracheyi* lightened the availability of seven important flavonoids namely 4',5 - dihydroxy, 6,7–dimethoxyflavone, Kaempferol - 3 - O - α - L – rhamnopyranoside, Quercetin - 3 - O - α - L – rhamnopyranoside, Kaempferol, Quercetin, Luteolin -7-O-glucoside A and Acacetin-7-O- α - L – rhamnopyranoside (Joshi and Verma, 2012). Phytochemicals, for example, free anthraquinone, ascorbic acid, sugars, phenolics, saponins and steroids were accounted to be available by Khan *et al*. (2009). The water and ethyl acetate derivation extricates likewise uncovered the presence of amino acids, carbohydrates, glycosides, and phenolic compounds. Chloroform extract affirmed the existence of steroids. Terpenoids were available in the ether concentrate of *B. stracheyi*. The results show the presence of amino acids, proteins, carbohydrates, glycosides, phenolics, steroids, and terpenoids in *B. stracheyi* (Kumar and Tyagi, 2013b). Two new bioactive bergenin derivatives, named as bergecins A and B, were also isolated. Both the compounds inhibited the Lipoxygenases enzyme in a concentration-dependent fashion with IC50 values of 49.78 mm and 24.3 mm, respectively (Siddiq *et al*., 2012). In mammalian cells, it is discovered that lipoxygenase items assume a part in an assortment of problems like inflammation (Nie and Honn, 2002) and bronchial asthma (Schneider and Bucar, 2005). Lip-oxygenases, therefore, are a potential target for the rational drug design and discovery of mechanism-based inhibitors for the treatment of autoimmune diseases, bronchial asthma, cancer and inflammation (Maharvi *et al*., 2008).

Scope for application in food industry

Food processors, regulatory agencies and food handling analysts have progressively been worried about the developing number of extreme foodborne episodes brought about by microorganisms like *Bacillus cereus*, *Staphylococcus aureus*, *Salmonella* sp., *Clostridium perfringens*, *Campylobacter*,

Listeria monocytogenes, *Vibrio para-haemolyticus*, *and* entero-pathogenic *Escherichia coli* (Wilson and Droby, 2000; Friedman *et al*., 2002). These microbes, causing over 90% of all food poisoning cases, have a Spartan army of a multitude of commercial antibiotics and food added substances to control them from causing sicknesses in (Wilson and Droby, 2000). These may cause severe hypersensitivity reactions and take us a step forward to one thing we are trying to avoid, antibiotic resistance. Alongside the danger of drug resistance and other infection-related phenomena, the purchaser's developing interest in food, liberated from brutal synthetic food-added substances and presence of an insignificant measure of unsafe additives with guaranteed quality and wellbeing, traditional means for controlling microbial deterioration and security risks in food varieties, are being supplanted by mixes of inventive advancements, that include natural antimicrobial substance, free of potential health hazard (Mukherjee *et al*., 2020). Numerous essential oils from plants used in Sidha and Ayurveda are utilized as a viable antimicrobial specialist and flavorings also, in the food business (Satyavani *et al*., 2015). The balance today tilts towards the side where natural food ingredients are used in place of presently available synthetic antioxidants. Thus, the synergism of flavor and antimicrobial potential along with antioxidant potential will skyrocket the natural agent utilization (Lis Balchin *et al*., 1998). The primary constituents of essential oils of the therapeutic plants and herbs belonging to the aromatic group are mono and sesquiterpenes including alcohols, aldehydes, carbohydrates, ethers, ketones, and phenols, and are answerable for the biological activity of medicinal plants as well as for their scent (Pandey *et al*., 2017). These properties have had the spices and herbs being added to food framework since ancient time, both as flavor enhancing specialists and also as preservatives (Kalemba and Kunicka, 2003). Because of essence of the above ascribes, the *Bergenia* species found in India can conceivably be utilized in the worldwide business and moving food enterprises as a flavoring, seasoning additive and natural preservative agent; subsequently, further examination will be supported towards the utilization of this enchanted herb in different food models.

Conclusion

The deadliest illnesses that are caused today are either by free radicals or microorganisms. Foodborne microbial episodes from different sources are yet an essential concern worldwide and produce 90% of the ailments identified with the food business. The evolving new strains of microorganisms and antibiotic resistant pathogens have effectively made devastation to the scientific society. This has paved a new window to screen wellsprings of antimicrobial agents, particularly the natural antimicrobial substances. The current review would provide information about the effectiveness of the miraculous herb, *Bergenia* species, against different kind of ailments and the responsible potent therapeutic compounds. This review is the primary endeavour to assemble most extreme divided writing about the ethnobotany, ethnopharmacology and phytochemistry of the three *Bergenia* species viz. *Bergenia ciliata, Bergenia ligulata* and *Bergenia stracheyi*. This would bring nearer the connection between current information and the fables folk information coming through ages, to inspire future studies identifying with the revelation of new novel compounds and medications from the three species.

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Author's contribution: SK: Involved in conceptualization, writing- original draft preparation, data curation; SC: Engaged in supervision and editing; SN: Involved in software and investigation; KCD: Involved in reviewing and editing; PM: Involved in resources.

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