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A REVIEW ON PHYTOCHEMICALS AND BIOLOGICAL PROPERTIES OF PLANT EXTRACTS OF *CRYPTOCARYA* SPECIES

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ABSTRACT
The genus *Cryptocarya* has been comprehensively examined for its diverse phytochemical composition, leading to the identification of numerous bioactive compounds. A study on *Cryptocarya impressinervia* identified 23 known compounds, including lignans, flavonoids, sterols, and triterpenoids, with *9,9'-O-Di-feruloyl-(-)-secoisolariciresinol* exhibiting potent cytotoxicity against five cancer cell lines in human (IC50: 3.58–6.39 µM). *Rhusemialin A* also showed potent action against HL-60 leukemia cells (IC50: 3.69 µM). From *Cryptocarya chinensis*, four novel flavanones (cryptoflavanones A–D) and known compounds such as pinocembrin and cryptocaryone demonstrated antituberculosis activity (MIC: 3.5 mg/mL and 25.0 mg/mL, respectively). *Cryptocarya myrtifolia* yielded cryptocaryalactone and its derivatives, while *C. obovata* provided cytotoxic flavonoids and R-pyrones, with obolactone and obochalcolactone exhibiting significant activity against the KB cancer cell line. Further investigations on *Cryptocarya wightiana* contributed to the isolation of a new lactone with germination-inhibitory properties and a high-viscosity polysaccharide gum, composed mainly of arabinose and xylose, with potential industrial applications. *Cryptocarya rugulosa* produced rugulactone, which effectively inhibited NF-κB signaling, a crucial cancer target. Additionally, *Cryptocarya alba* was found to contain phenolics and flavonoid compounds with strong antioxidant activity. Antimicrobial studies on *Cryptocarya* extracts showed significant inhibition of formation of *Candida albicans* biofilm but also cytotoxic effects on normal oral keratinocytes. The antioxidant potential of *C. stocksii* was assessed through DPPH, reducing power, and total antioxidant assays, where ethanol extracts demonstrated the highest activity, attributed to high polyphenol content. These findings highlight the potential of *Cryptocarya* species as sources of cytotoxic, antimicrobial, and antioxidant compounds, paving the way for their application in pharmaceutical and industrial fields.

KEYWORDS: *Cryptocarya*, Phytochemicals, Cytotoxicity, Antimicrobial, Antioxidant.

INTRODUCTION
Plants were a gift from nature, and they have therapeutic properties for all living things. Numerous plants were identified to have therapeutic characteristics and are being utilized in traditional medicine to treat ailments and disorders globally.[1] The process of discovering and creating novel medications, natural compounds, and/or their structures is extremely important.[2] Plant chemicals are now the main ingredient used by pharmaceutical companies to make about one-fourth of their medications. In order to find possibilities for therapeutic usage, medicinal plants were evaluated for active components that may fight off illnesses, cancer, wounds, and germs.[3] The pharmaceutical sector has recently employed its resources and time to produce natural medications that are unknown to the general public.[4, 5] Phytochemicals, as the word suggests, they are the individual compounds from which plants are made.[6]

The genus *Cryptocarya* belongs to the family Lauraceae is comprised of more than 350 species dispersed across the world's temperate, tropical, and subtropical regions.[7] Several Lauraceae plants have been studied for their biological traits and chemical phytoconstituents because of their commercial significance. Many of the Lauraceae species have been utilized in the manufacture of various products of high economic worth in areas such as the food and wood industries.[8] *Cryptocarya* species is a moderately sized tree that thrives up to 20m tall. *Cryptocarya* species are reported to generate a wide variety of intriguing bioactive phytochemicals, including alkaloids.[9] The pharmacological properties of *Cryptocarya* components, including as their anti-inflammatory, antimalarial, antitrypanosomal, and cytotoxic properties, have garnered significant attention.[10] Additionally, most *Cryptocarya* trees are known for their extremely precious timbers.[11] Cancer is a terrifying illness that ranks second in terms of causes of death, after heart disease. Cancer claims the lives of around 3.5 million people annually.[12] Several strategies are employed to combat this illness, such as the usage of natural substances as anti-cancer medications. Since natural chemicals are derived from diverse and renewable resources, they have proven to be one of the most promising medical sources. Plants of the Lauraceae family are among the many higher plants that may contain anti-cancer chemicals. *Cryptocarya* is one genus in the Lauraceae family that has been traditionally used as a medicine to relieve pain.[13]

TAXONOMIC DESCRIPTION OF *CRYPTOCARYA* R. BR.

Kingdom: Plantae
Clade: Angiosperms
Clade: Magnoliids
Order: Laurales
Family: Lauraceae
Genus: *Cryptocarya* R. Br.

Morphological Characteristics

1) **Habit**: Evergreen trees or shrubs, occasionally reaching up to 30–40 meters in height.
2) **Leaves**: Alternate or spiral arrangement. Pinnately veined, with some species exhibiting three veins at the base. Reticulate venation, often with a distinct areolate pattern.[14]
3) **Inflorescence**: Cymose, racemose, or paniculate, typically axillary and often appearing terminal.
4) **Flowers**: Bisexual, small (2–3 mm long and 1–2 mm wide in dried specimens). Six perianth segments (tepals) in two whorls. Nine stamens in three whorls; the inner whorl often with staminodes. Anthers two-locular, dehiscing by valves. Ovary superior, seated within a distinct and deep hypanthium.[14]
5) **Fruit**: A drupe, often fleshy, enclosed by the persistent and expanded hypanthium, resulting in an inferior fruit. Shape varies from elliptic to spherical.
6) **Bark**: Typically, smooth or slightly fissured. Rich in aromatic compounds, with some species being sources of essential oils.[11]

Distribution and Habitat

- *Cryptocarya* is a pantropical genus, with species distributed across the Neotropical, Afrotropical, Indomalayan, and Australasian regions.
- In India, species are primarily found in the Western Ghats, Northeastern states, and the Andaman & Nicobar Islands.
- Habitats include tropical evergreen forests, montane forests, and subtropical regions.[15]

Economic and Ecological Importance

- Several species are sources of essential oils with potential medicinal properties.[11] Fruits serve as a food source for various fauna, playing a role in forest ecology.

Distribution of Genus *Cryptocarya* in India

According to Gangopadhyay and Chakrabarty (2005)[16], there are 15 species of *Cryptocarya* R. Br. (Lauraceae) in the Indian subcontinent, which encompasses Bangladesh, Myanmar, Nepal, Bhutan, Sri Lanka, and India. For every species, their research yielded comprehensive morphological descriptions, distribution patterns, and ecological notes. Native to the Agasthyamalai, Periyar, and Anamalai areas of the southern Western Ghats of India, *Cryptocarya anamalayana* thrives at elevations ranging from 1,000 to 1,400 meters. *Cryptocarya wightiana* is found in the Western Ghats, especially in the South and Central Sahyadris, Sri Lanka, and Myanmar. It prefers evergreen forests that are up to 900 meters high, and sometimes as high as 1,200 meters. Throughout the Andaman Islands and the northeastern states of Meghalaya, Assam, Sikkim, West Bengal, and Arunachal Pradesh, as well as Bhutan, Nepal, Tibet, Thailand, Bangladesh, Myanmar Malaysia, and Sumatra, *Cryptocarya* amygdalina can be found living in tropical forests that range in elevation from 300 to 1,350 meters. So far, only reports have indicated roughly ten unique trees of *Cryptocarya muthuvariana*, which was recently found in Edamalakkudy, Idukki district, Kerala. At an elevation of roughly 1,100 meters, the southern Western Ghats of Kerala, which include Sheikelmudi and Malakkappara, are home to *Cryptocarya sheikelmudiyana*. The Middle and other Andaman Islands are home to *Cryptocarya ferrarsi* and *Cryptocarya caesia*. Although from Java *C. caesia* was first reported and it is currently present in places like Port Blair and Mount Harriet National Park. The Western Ghats in Tamil Nadu and Kerala are the primary locations for reports of *Cryptocarya beddomei* and *Cryptocarya lawsonii*. *Cryptocarya bourdillonii* is native to Kerala's Western Ghats, whilst *Cryptocarya andamanica* is indigenous to the Andaman Islands. Two locations for *Cryptocarya floribunda* are the Western Ghats and Sri Lanka. In Assam and Meghalaya, *Cryptocarya griffithii* is primarily found. Only the southern Western Ghats of Kerala are home to *Cryptocarya travancorica*, while *Cryptocarya stocksii* is found throughout the Western Ghats, particularly in Karnataka and Maharashtra.

CHEMICAL CONSTITUENTS OF *CRYPTOCARYA* SPECIES AND THEIR PHARMACOLOGICAL ACTIVITY

Cytotoxic Lignans from *Cryptocarya impressinervia*

A chemical evaluation of the twigs of *Cryptocarya impressinervia* resulted in the identification of 23 known compounds. These included eight lignans, three phenylpropionates, one xanthone, three flavonoids, one phenylpropanoid, one substituted phenol, one triterpenoid, three sterols, and two aliphatic compounds. This study marks the very first instance of these compounds being derived from *C. impressinervia*. Among them, 9,9'-O-Di-feruloyl-(-)-secoisolariciresinol (compound 1) showed strong cytotoxic effects against five human cancer cell lines—HL-60, SMMC-7721, A-

549, MCF-7, and SW-480—with IC50 values of 3.58, 4.55, 6.39, 5.09, and 4.80 µM, respectively. Another compound, Rhusemialin A (compound 2), showed strong activity against HL-60, with an IC50 of 3.69 µM. Dihydrosinapyl ferulate (compound 3) demonstrated moderate cytotoxicity across all the five tested cancer cell lines. To date, this is the preliminary report detailing both the chemical compounds of *C. impressinervia* and the cytotoxic effect of these three compounds.[2]

New Flavanones from *Cryptocarya chinensis* and Their Antituberculosis Activity

Four novel flavanones, designated as cryptoflavanones A–D (compounds 1–4), were extracted from the leaves of *Cryptocarya chinensis*, in addition to previously known eight compounds. Structural analysis of these newly discovered flavanones was conducted by making use of spectral techniques. Notably, two of the isolated compounds, pinocembrin (compound 5) and cryptocaryone (compound 6), possessed antituberculosis properties effective against *Mycobacterium tuberculosis* H37Rv in vitro, showing minimum inhibitory concentration (MIC) values of 3.5 mg/mL and 25.0 mg/mL, respectively.[17]

α-Pyrones along with Their Derivatives from Two *Cryptocarya* Species

The species *Cryptocarya myrtifolia* was found to contain *Cryptocarya*lactone and its deacetyl derivative, that had been earlier identified only once before. Additionally, a newly discovered compound, 7-styryl-2,6-dioxabicyclo [3,3,1] nonan-3-one, was isolated. This cyclic compound was also synthesized through a simple transformation of deacetyl*Cryptocarya*lactone. Other compounds obtained from *C. myrtifolia* included cryptofolione and a trace oxidation product.[18]

Cytotoxic Flavonoids and α-Pyrones from *Cryptocarya obovata*

From the fruits and trunk bark of *Cryptocarya obovata*, five compounds were isolated, including one α-pyrone (obolactone, compound 1), two chalcones (kurzichalcolactone B, compound 2, and obochalcolactone, compound 3), and two flavanones (oboflavanones A and B, compounds 4 and 5). Spectroscopic techniques were used to determine the structures of these novel compounds. The absolute configuration of obolactone (compound 1) was validated using circular dichroism analysis. Both obolactone (compound 1) and obochalcolactone (compound 3) displayed significant cytotoxicity in vitro against the KB cancer cell line. Additionally, potential biosynthetic pathways for oboflavanones and obochalcolactone were proposed.[19]

***Lauraceae* Alkaloids**

The *Lauraceae* family is recognized as one of the most diverse botanical families, comprising 67 genera and over 2,500 species. More than 300 different alkaloids, primarily isoquinolines, have been documented within this family. The significance of these alkaloids, along with their role in chemosystematic relationships, has been extensively discussed.[8]

A New *Cryptocarya* lactone

A newly identified lactone compound, 6-({4-oxo-6-[(1E)-2-phenylvinyl]-2H-3,5,6-trihydropyran-2-yl} methyl)-5H-6-hydropyran-2-one ($C_{19}H_{24}O_4$), has been isolated from the seeds of *Cryptocarya wightiana*. This compound acts as a germination inhibitor, influencing seed growth and development.[20]

Isolation and Partial Characterization of a Polysaccharide Gum from *Cryptocarya wightiana* Bark

A gummy polysaccharide was extracted and partially characterized from the bark of *Cryptocarya wightiana*. This polysaccharide exhibited high viscosity and 'pituity' properties, indicating potential industrial applications. Compositional analysis revealed that it mainly consists of arabinose and xylose in a 6:1 ratio. Fractionation using alcohol precipitation yielded four individual fractions having different compositions and viscosity characteristics. The primary fraction, constituting 58% of the total extract, contained arabinose and xylose in a 5:1 ratio, along with an unidentified peak (~21%) eluting alongside arabinose. Due to its unique properties, this gum has potential applications in both food and non-food industries.[21]

Antimicrobial Efficacy and Biocompatibility of Extracts from *Cryptocarya* Species

This research focused on evaluating the antimicrobial potential of *Cryptocarya* extracts against *Candida albicans* biofilm and their biocompatibility. The study involved forming a mature *C. albicans* biofilm on denture base acrylic resin samples. The fungicidal effects of the extracts were assessed through the Alamar Blue® assay, colony-forming unit (CFU/mL) counting, and confocal laser scanning microscopy (CLSM). Cytotoxicity was examined using the Alamar Blue® assay on normal oral keratinocytes (NOK) cells. Additionally, ultra-high-performance liquid chromatography coupled with a diode array detector and tandem mass spectrometry (UPLC-DAD-MS) was used for plant extract analysis. Results indicated a significant decrease in cellular metabolism and CFU/mL count of *C. albicans* ($p<0.05$), with a concentration of 0.045 g/mL completely inhibiting CFU/mL formation. Although all extracts demonstrated antimicrobial activity, they also exhibited cytotoxic effects on NOK cells.[22]

Inhibitors of the NF-κB Activation Pathway from *Cryptocarya rugulosa*

The nuclear factor-κB (NF-κB) signaling pathway plays a crucial role in various cancers, making it a potential therapeutic target. A cell-based assay assessing the stability of inhibitor of kappa B (IκB), a key NF-κB regulator, revealed that an organic solvent extract of *Cryptocarya rugulosa* suppressed constitutive NF-κB activity in human lymphoma cell lines. The active compounds were identified as rugulactone, a newly discovered α-pyrone, and the previously known cryptocaryone. Rugulactone exhibited the most potent activity, increasing IκB levels up to fivefold at 25 µg/mL, with the highest activity observed after a 10-hour exposure.[23]

Antioxidant Capacity and HPLC-DAD-MS Profiling of Chilean *Cryptocarya alba* Fruits and Comparison with *Crataegus monogyna*

High-performance liquid chromatography (HPLC) with UV detection and electrospray ionization tandem mass spectrometry (ESI-MS/MS) was used to analyze the phytochemical profile of *Cryptocarya alba* (*Chilean peumo*) and *Crataegus monogyna* (*German peumo*) from southern Chile. A total of 33 compounds were identified, including flavonoid glycosides, phenolic acids, anthocyanins, and flavonoid aglycones, with 19 detected in *C. alba* and 23 in *C. monogyna*. Quantification of total flavonoid and phenolic content revealed higher levels in *C. monogyna* than in *C. alba*. The antioxidant capacity of *C. alba* fruits was measured at 9.12 ± 0.01 µg/mL using the DPPH assay, which was approximately triple the amount lower than *C. monogyna* (3.61 ± 0.01 µg/mL).[24]

Isolation and Characterization of Pharmacologically Active Components from *Cryptocarya stocksii* and *Nardostachys jatamansi*

DPPH Scavenging Activity

The DPPH radical scavenging assay was used to evaluate the antioxidant potential of different extracts. Ascorbic acid, the standard reference, exhibited strong radical scavenging activity, while the ethanol extract demonstrated a concentration-dependent scavenging effect with an IC50 of 41 µg/mL. Among the tested extracts, ethanol extract showed the highest scavenging activity (81% at 100 µg/mL), followed by chloroform (67.7%) and petroleum ether extracts (35%), in comparison to ascorbic acid (96.2%).

Reducing Power Assay

The reducing power assay was used to evaluate the ability of *C. stocksii* stem bark extracts to reduce Fe3+ to Fe2+, indicative of antioxidant potential. The ethanol extract showed the highest reduction of ferricyanide (Fe3+) complex, as indicated by increased absorbance at 700 nm, followed by chloroform and petroleum ether extracts. This suggests that the antioxidant compounds in the ethanol extract play a significant role in reducing oxidative stress.

Total Antioxidant Activity

The total antioxidant capacity was determined using the phosphomolybdenum assay, which measures the reduction of Mo (VI) to Mo (V) and the formation of a green phosphate/Mo (V) complex with maximum absorption at 695 nm. Among the tested extracts, the ethanol extract exhibited the highest antioxidant activity (0.9 mg/100 mg), followed by the chloroform extract (0.43 mg/100 mg) and the petroleum ether extract (0.29 mg/100 mg). The superior antioxidant capacity of the ethanol extract was attributed to its high polyphenol content, as these compounds play a vital role in scavenging free radicals and protecting biological systems from oxidative damage.[25]

The many species of *Cryptocarya*, their extracts, discovered chemicals, and biological activity are compiled in Table 1. Solvents such methanol, ethanol, and water were used to extract different plant components, including bark and leaves. Alkaloids, flavonoids, terpenoids, and polysaccharides were among the bioactive substances identified in the extracts. Polysaccharides in *Cryptocarya wightiana* bark extract, for instance, caused it to exhibit high viscosity and pituity, suggesting potential for use in medicine. Several species demonstrated cytotoxic, antibacterial, anti-inflammatory, and antioxidant properties, underscoring the genus' therapeutic potential.

Table 1: Different species of *Cryptocarya*, their extracts, identified compounds and its biological activity.

Name of the plant	Plant parts used	Solvents used	Identified compound	Biological activity	References
Cryptocarya impressinervia	Twigs	Methanol and Ethyl acetate	Lignans (e.g., 9,9'-O-Di-feruloyl-(-)-secoisolariciresinol), Rhusemialin A, Dihydrosinapyl ferulate	Cytotoxicity against 5 human cancer cell lines	[2]
Cryptocarya chinensis	Leaves	Chloroform	Flavanones (Cryptoflavanones A–D), Pinocembrin, Cryptocaryone	Antituberculosis activity	[17]
Cryptocarya myrtifolia	Leaves	Dichloromethane (CH_2Cl_2), Hexane, Ethyl Acetate, Methanol (for purification)	*Cryptocarya*lactone, Deacetyl*Cryptocarya*lactone, 7-styryl-2,6-dioxabicyclo[3,3,1]nonan-3-one, Cryptofolione	γ-Pyrones and derivatives	[18]
Cryptocarya obovata	Fruits and trunk bark	Ethanol	Obolactone, Kurzichalcolactone B, Obochalcolactone, Oboflavanones A and B	Cytotoxicity against KB cancer cell line	[19]

Cryptocarya wightiana	Seeds	Hexane and Ethyl acetate	New lactone (germination inhibitor)	Germination inhibition	[20]
Cryptocarya wightiana	Bark	Aqueous extraction (alcohol precipitation for fractionation)	Polysaccharide gum (mainly arabinose and xylose)	Industrial applications (high viscosity properties)	[21]
Cryptocarya rugulosa	Leaves, Twigs	Water, Methanol, Hexane	Rugulactone, Cryptocaryone	NF-κB pathway inhibition, anticancer potential	[23]
Cryptocarya alba	Fruits and Leaves	Methanol and others (for HPLC-DAD-MS)	Flavonoid glycosides, Phenolic acids, Anthocyanins, Flavonoid aglycones	Antioxidant activity (DPPH assay)	[24]
Cryptocarya moschata, *Cryptocarya mandioccana*, *Cryptocarya saligna*	Leaves trunk, bark and fruit	Hydroalcoholic solvent (water 30% and ethanol 70%)	**Flavonoids** • Quercetin-3-O-glycosides (Compounds 3–7) • Trimethylquercetin (Compound 11) **Aporphine Alkaloids** • Menisperine (Compound 1) • Xanthoplanine (Compound 2) **Styrylpyrones** • Goniothalamine (Compound 8) – Found only in *C. moschata* • 6-Styryl-2-pyrone (Compound 9) – Found only in *C. moschata* • Deacetyl*Cryptocarya*lactone (Compound 10) – Found only in *C. mandioccana*	Antimicrobial activity against *Candida albicans*, cytotoxicity on NOK cells	[22]

Applications of *Cryptocarya* species

1. Source of bioactive phytochemicals such as alkaloids with anti-inflammatory, antimalarial, antitrypanosomal, and cytotoxic properties.[10]
2. Source of highly valuable timber.[11]
3. Pain relief in traditional medicine.[13]
4. Cytotoxic compounds isolated from *Cryptocarya impressinervia* shows effectiveness against human cancer cell lines.[2]
5. Antituberculosis activity of flavanones isolated from *Cryptocarya chinensis*.[17]
6. Isolation of α-pyrones and derivatives with potential biological activities from *Cryptocarya myrtifolia*.[18]
7. Cytotoxic flavonoids and α-pyrones isolated from *Cryptocarya obovata* exhibit significant cytotoxic effects targeting cancer cell lines.[19]
8. Presence of diverse alkaloids (especially isoquinoline types) in *Cryptocarya* species, important for pharmacological and chemotaxonomic studies.[8]
9. Seed germination inhibitor compound (a new lactone) isolated from *Cryptocarya wightiana*.[20]
10. Polysaccharide gum extracted from *Cryptocarya wightiana* bark with potential applications in food and non-food industries.[21]
11. Antimicrobial activity against *Candida albicans* biofilm, though showing some cytotoxicity towards normal oral keratinocytes.[22]
12. Inhibition of the NF-κB signaling pathway by compounds from *Cryptocarya rugulosa*, suggesting potential anticancer therapeutic applications.[23]
13. Antioxidant properties of fruits of *Cryptocarya alba* (Chilean peumo).[22]

Over 350 species make up the genus *Cryptocarya* (Lauraceae), many of which have not been fully studied for their pharmacological and phytochemical characteristics. Many *Cryptocarya* species are ecologically important, although many have not received scientific investigation. Several species, including *Cryptocarya anamalayana*, *Cryptocarya muthuvariana*, *Cryptocarya sheikelmudiyana*, *Cryptocarya ferrarsi*, *Cryptocarya andamanica*, *Cryptocarya bourdillonii*, *Cryptocarya lawsonii*, *Cryptocarya travancorica*, and *Cryptocarya griffithii*, have not yet been the subject of phytochemical, pharmacological, or biological studies, according to comprehensive literature reviews and international botanical records. These species offer important chances for groundbreaking scientific research because, usually they are mostly found in the Andaman Islands and Western Ghats. Research on these species may greatly advance our knowledge, potential medical applications of the genus and aid in the development of new bioactive chemicals.

FUTURE PROSPECTUS

The various pharmacological characteristics of *Cryptocarya* species, such as their antibacterial, antioxidant, and anticancer effects, which are highly promising. Presence of bioactive substances like alkaloids, lignans, and flavonoids demonstrating great promise in the therapy of a range of illnesses, more investigation may result in the creation of new therapeutic agents. Furthermore, their use in sectors like food, cosmetics, and agriculture—particularly through the use of polysaccharides—creates chances for environmentally friendly and sustainable solutions. Further research into these species may lead to improvements in the industrial and pharmacological domains.

CONCLUSION

A notable source of pharmacologically active natural compounds is the genus *Cryptocarya* (Lauraceae), which includes a variety of plants found in tropical and subtropical areas, including India's Western Ghats. Many studies have confirmed that *Cryptocarya* species are abundant in bioactive phytochemicals, including polysaccharides, alkaloids, flavonoids, lignans, and α-pyrones. Many of these compounds have strong anti-inflammatory, antioxidant, cytotoxic, and antibacterial properties. The therapeutic potential of these substances, especially in the treatment of infectious diseases and cancer, emphasizes how important *Cryptocarya* is to current drug discovery initiatives. Further highlighting the need for the genus's conservation and more thorough phytochemical research is its ecological and economic relevance. The identification of new, naturally present bioactive substances with significant pharmacological potential is made possible by the ongoing study of *Cryptocarya* species.

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Author Contribution

Monisha C Patil: Original draft writing, conceptualization, data curation, methodology, resources, review and editing. **Govindappa M**: Final draft analysis, investigation, visualization, supervision.

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Data availability

Data will be made available on request.

Code availability

Not applicable.

Declarations

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