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Review Article

HELICHRYSUM PETIOLARE HILLIARD AND B. L. BURTT: A REVIEW OF ITS MEDICINAL USES, PHYTOCHEMISTRY, AND BIOLOGICAL ACTIVITIES

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ABSTRACT

Helichrysum petiolare is a valuable and well-known medicinal herb in South Africa. A comprehensive review of phytochemical, medicinal uses, and biological activities of *H. petiolare* is presented in this study. Information on biological activities, medicinal uses, and phytochemistry of *H. petiolare* was gathered from several internet sources which included Scopus, Google Scholar, Elsevier, Science Direct, Web of Science, PubMed, SciFinder, and BMC. Additional information on these aspects was sourced from pre-electronic sources such as journal articles, scientific reports, theses, books, and book chapters obtained from the University library. The current study revealed that *H. petiolare* is mainly used as herbal medicine for respiratory infections, diabetes, fever, headache, heart problem, high blood pressure, pain, reproductive problems, and wounds. Phytochemical studies showed that *H. petiolare* extracts and compounds isolated from the species have antifungal, anti-inflammatory, antibacterial, antioxidant, antityrosinase, antigenotoxicity, and cytotoxicity activities. This research showed that *H. petiolare* is an integral part of indigenous pharmacopeia in South Africa, but there is the lack of alignment between the known medicinal applications, phytochemistry, and biological activities of the species. Therefore, future research should focus on evaluating the chemical and pharmacological properties of *H. petiolare* extracts and compounds associated with the species.

Keywords: *Asteraceae*, *Helichrysum petiolare*, Ethnopharmacology, Herbal medicine, Southern Africa.

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INTRODUCTION

Helichrysum petiolare Hilliard and B. L. Burtt is a small shrub which is a member of the Asteraceae or Compositae family. The species is endemic to South Africa, confined to the Free State, Western Cape, Eastern Cape, and Northern Cape Provinces [1-6]. The species is commonly known by several vernacular names which include the following: Bedding *Helichrysum*, cudweed everlasting, herbal *Helichrysum* and silver bush everlasting (English), hottentotskooigoed, hottentotskruie, kooigoed, and kruie (Afrikaans), and imphepho (Xhosa) [7-11]. A single synonym "*Helichrysum petiolatum* auct. non (L.) DC." was found in literature [1-5]. The genus name "*Helichrysum"* is based on the Greek word "*helios" which translates to* "sun" and "*chrysos"* which translates to "gold," in reference to "golden flowers" which are characteristic of the genus [11]. The species name, "*petiolare" is in reference* to long leaf stalks which are a characteristic feature of the species *H. petiolare* [11]. The height of *H. petiolare* ranges from 30 to 120 cm, has been recorded in drier inland sheltered slopes in the fynbos biome, transition zones, and forest margins at an altitude ranging from 120 to 1420 m above sea level [1-6,11]. *H. petiolare* is a perennial scrambling or trailing shrub with dense, aromatic, roundish to ovate, green-yellowish leaves covered by silver-gray hairs [2,11]. The inflorescence is made up of many tiny yellow flowers forming small flower heads, surrounded by creamy white and papery floral bracts on long stalks. The seeds of *H. petiolare* are small, lightweight, with tuft of bristly hairs at one end and are dispersed by wind [11].

H. petiolare is an important ornamental plant in Namibia, South Africa, North Africa, Europe, and the United States of America [11-21]. The species is attractive and has been sold in specialty nurseries as an ornamental plant throughout the world [12]. *H. petiolare* is now listed as a weed in the global collection of weeds by Randall [22] and Mouriño *et al*. [23] described the species as an invasive species in Spain, invading natural and semi-natural habitats as well as managed afforested areas and maritime protected areas. In the USA, *H. petiolare* is listed as an invasive weed, invading coastal scrubland and conifer forests [24]. Based on literature records, *H. petiolare* is naturalized as a casual or invasive weed in France, North Africa, New Zealand, Portugal, Spain, Sweden, the UK, and the USA [13,14,20,23,25-30]. The species was first recorded as naturalized in the Iberian Peninsula in Portugal in 1943 [30] and by 1952, the species was widespread in Portugal as a weed, established in natural or semi-natural communities [31]. *H. petiolare* was introduced in the USA as an ornamental herb [12] and escaped from cultivation in areas like California around 1960 [12,24,32,33]. The current study is focusing on the medicinal applications of the species and its contribution to primary health care of local communities. Therefore, the current study is aimed at providing a comprehensive review of ethnomedicinal value, phytochemistry, and biological activities of compounds isolated from the species, including *H. petiolare* crude extracts.

MEDICINAL USES OF *H. PETIOLARE*

Research by Oliver [11] showed that *H. petiolare* is one of the best known and commonly used herbal medicines in South Africa. Similarly, Van Wyk *et al*. [34] listed *H. petiolare* as one of the popular *Helichrysum* species used as herbal medicines against menstrual pain, colds, coughs, infections, headache, and fever in South Africa. Other *Helichrysum* species with medicinal applications similar to those of *H. petiolare* are *Helichrysum aureonitens* Sch. Bip., *Helichrysum nudifolium* (L.) Less., *Helichrysum odoratissimum* (L.) Sweet, *Helichrysum pedunculatum* Hilliard and B. L. Burtt, and *H. cymosum* (L.) D. Don [35-60]. Research by Loundou [61] revealed that leaves and stems of *H. petiolare* are sold in the informal herbal medicines markets of the Eastern Cape and Western Cape Provinces of South Africa as herbal medicines. The leaves, twigs, whole plant parts, or sometimes roots are used as herbal medicines for mainly respiratory infections, diabetes, fever, headache, heart problem, high blood pressure, pain, reproductive problems, and wounds as indicated in Table 1.

BIOLOGICAL ACTIVITIES

H. petiolare contain a diversity of terpenoids and non-terpenoids (Table 2) that have been identified from the flowers, leaves, and twigs of the species [63,69-71]. The major compounds that have been identified

Table 1: Medicinal uses of *H. petiolare* in South Africa

Disease	Parts used	References
Antiseptic	Leaves	[11,62]
Asthma	Leaves	[10,11,63]
Catarrh	Leaves	[62,64]
Chest problems	Leaves	[10,11,63]
Colds	Leaves	[11,62-64]
Cough	Leaves	[11,62-64]
Diabetes	Whole plant	[65-68]
Fever	Whole plant	[62,64]
Headache	Whole plant	[62,64]
Heart problems	Whole plant	[17]
High blood pressure	Leaves	[10,11,63]
Infections	Leaves	[10,11]
Insect repellent against flies and mosquitos	Leaves mixed with those of *Artemisia afra* Jacq. ex Willd	[11]
Menstrual problems	Whole plant	[62,64]
Respiratory problems	Leaves	[10]
Pain	Leaves	[11,63]
Urinary tract infections	Whole plant	[62,64]
Wounds	Leaves	[10,11,62,64]

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from the species include β-bisabolene (19.5–25.6%), α-bulnesene (19.5–25.6%), caryophyllenyl alcohol (36.4–45.3%), 1,8-cineole (<0.01–22.4%), β-hydroagarofuran (19.5–25.6%), and β-pinene (<0.01–51.3%) [63,69,70].

BIOLOGICAL ACTIVITIES

The following biological activities have been reported from *H. petiolare* crude extracts and essential oils extracted from the species: Antibacterial [62,69,70,72], antifungal [62], antioxidant [69], antityrosinase [73], anti-inflammatory [69], antigenotoxicity [74], and cytotoxicity [72] activities.

Antibacterial activities

Lourens *et al*. [69] evaluated antibacterial activities of acetone and methanol leaf extracts and essential oils of *H. petiolare* against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus cereus*, *Bacillus subtilis*, *Yersinia enterocolitica,* and *Klebsiella pneumoniae* using disc diffusion assay and microtiter plate dilution method with neomycin (30 µg/disc) as the positive control. The acetone and methanol extracts exhibited activities against *S. aureus* and *B. cereus* with zone of inhibition ranging from 2.5 mm to 9.0 mm, while the essential oil was

Table 2: Phytochemical composition of *H. petiolare*

Phytochemical composition (%)	Values	Plant parts	References
Ar-curcumene	0.6	Leaves	[69]
Allo-aromadendrene	0.6–0.8	Flowers, leaves, and twigs	[63]
Aromadendrene	0.3	Aerial parts and leaves	[69,70]
α-trans-Bergamotene	0.2	Flowers	[63]
β-Bisabolene	19.5–25.6	Flowers, leaves, and twigs	[63]
α-Bisabolol	0.3	Flowers, leaves, and twigs	[63]
epi-α-Bisabolol	0.2	Flowers, leaves, and twigs	[63]
β-Bisabolol	0.8	Aerial parts and leaves	[69,70]
Borneol	<0.1–3.3	Flowers, leaves, and twigs	[63,69,70]
Bornyl acetate	<0.1–0.5	Flowers, leaves, and twigs	[63]
α-Bulnesene	19.5–25.6	Flowers, leaves, and twigs	[63]
Cubenol	0.3	Flowers, leaves, and twigs	[63]
Cadalene	0.2–0.3	Flowers, leaves, and twigs	[63]
trans-Cadina-1,4-diene (Cubebene)	<0.1	Flowers, leaves, and twigs	[63]
α-Cadinene	<0.01	Flowers, leaves, and twigs	[63]
δ-Cadinene	0.7–4.8	Aerial parts, flowers, leaves, and twigs	[63,69,70]
trans-y-Cadinene	0.3	Flowers	[63]
epi-α-Cadinol	0.8–3.9	Flowers, leaves, and twigs	[63]
α-Cadinol	0.2	Aerial parts and leaves	[69,70]
T-Cadinol	0.2	Aerial parts and leaves	[69,70]
α-Calacorene	0.1–1.6	Aerial parts, flowers, leaves, and twigs	[63,69,70]
Cis-calamenene	0.3	Leaves	[69]
Calamenene	0.3	Aerial parts	[70]
Camphene	<0.01–0.4	Aerial parts, flowers, leaves, and twigs	[63,69,70]
α-Campholenal	0.1	Flowers, leaves, and twigs	[63]
Camphor	0.1–1.9	Aerial parts, flowers, leaves, and twigs	[63,69,70]
Carotol	0.1–1.1	Flowers, leaves, and twigs	[63]
Carvacrol	0.1	Aerial parts and leaves	[69,70]
trans-Carveol	0.1	Aerial parts and leaves	[69,70]
Caryophylladienol II	0.2–0.4	Aerial parts and leaves	[69,70]
Caryophyllenyl alcohol	36.4–45.3	Flowers, leaves, and twigs	[63]
β-Caryophyllene alcohol	1.9	Aerial parts and leaves	[69,70]
Caryophyllene oxide	0.1–2.5	Aerial parts, flowers, leaves, and twigs	[63,69,70]
β-Caryophyllene	0.3–14.0	Aerial parts, flowers, leaves, and twigs	[63,69-71]
Caryophyllenol-I	0.2	Aerial parts and leaves	[69,70]
Caryophyllenol-II	0.3	Aerial parts and leaves	[69,70]
β-Chamigrene	0.4–0.5	Flowers, leaves, and twigs	[63]
1,8-Cineole	<0.01–22.4	Aerial parts, flowers, leaves, and twigs	[63,69,70]
Clovenol	0.1	Aerial parts and leaves	[69,70]
α-Copaene	0.1–2.4	Aerial parts, flowers, and leaves	[63,69,70]
β-Copaene	0.2–0.4	Flowers, leaves, and twigs	[63]
1-epi-Cubenol	0.8–1.2	Flowers, leaves, and twigs	[63]
ar-Curcumene	0.6–0.7	Aerial parts, flowers, leaves, and twigs	[63,70]
p-Cymen-8-ol	0.3	Aerial parts and leaves	[69,70]
Cyperene	0.2	Flowers, leaves, and twigs	[63]

(Contd...)

Table 2: (*Continued*)

o-Cymene	<0.01–1.0	Flowers, leaves, and twigs	[63]
p-Cymene	9.8	Aerial parts and leaves	[69,70]
p-Cymenene = α, p-Dimethylstyrene	0.1	Aerial parts	[70]
(2E,4E)-Deca-2,4-dienal	0.1	Flowers, leaves, and twigs	[63]
Decanal	<0.1–1.4	Flowers, leaves, and twigs	[63]
(E)-2-Decenal	<0.1	Flowers, leaves, and twigs	[63]
1,10-Di-epi-cubenol	0.1–0.2	Flowers, leaves, and twigs	[63]
α, *p*-Dimethylstyrene	0.1	Leaves	[69]
cis-1,2-Epoxy-terpin-4-ol	0.4	Aerial parts and leaves	[69,70]
10-epi-y-Eudesmol	0.9–1.3	Flowers, leaves, and twigs	[63]
α-Fenchone	<0.01–0.7	Aerial parts and leaves	[69,70]
Fenchyl alcohol	1.5	Aerial parts and leaves	[69,70]
Geranyl acetate	0.1–0.4	Aerial parts and leaves	[69,70]
(E)-Geranyl acetate	0.1	Aerial parts and leaves	[69,70]
Germacrene D-4-ol	<0.1–2.3	Flowers, leaves, and twigs	[63]
Gleenol	<0.1	Flowers, leaves, and twigs	[63]
Globulol	0.2	Aerial parts and leaves	[69,70]
α-Guaiene	0.1–0.2	Flowers, leaves, and twigs	[63]
3,7-Guaiadiene	0.1–0.6	Aerial parts and leaves	[69,70]
Guaiol	<0.1–2.0	Flowers, leaves, and twigs	[63]
α-Gurjunene	<0.01–0.5	Aerial parts, flowers, leaves, and twigs	[63,69,70]
γ-Gurjunene	0.1	Aerial parts and leaves	[69,70]
1-Heptanol	0.1	Aerial parts	[70]
1-Hexanol	<0.01	Aerial parts	[70]
Hexyl valerate	<0.01	Aerial parts	[70]
Humulene epoxide I	0.1	Aerial parts and leaves	[69,70]
Humulene epoxide II	0.1–1.4	Aerial parts, flowers, leaves, and twigs	[63,69,70]
α-Humulene	2.0–3.8	Aerial parts, flowers, leaves, and twigs	[63,69,70]
β-Hydroagarofuran	19.5–25.6	Flowers, leaves, and twigs	[63]
Intermedeol	0.3–3.3	Flowers, leaves, and twigs	[63]
Isocaryophyllene oxide	0.6	Aerial parts and leaves	[69,70]
Isoitalicene	0.1	Aerial parts and leaves	[69,70]
Italicene	1.0	Aerial parts and leaves	[69,70]
Kaur-15-ene	0.3	Aerial parts and leaves	[69,70]
Kaur-16-ene	1.3	Aerial parts	[70]
Lavandulol	<0.1–0.1	Flowers, leaves, and twigs	[63]
Lavandulyl acetate	0.7–1.3	Flowers, leaves, and twigs	[63]
Lavandulyl isobutyrate	0.2–0.4	Flowers, leaves, and twigs	[63]
Lavandulyl isovalerate	1.9–2.5	Flowers, leaves, and twigs	[63]
Ledol	0.2	Aerial parts and leaves	[69,70]
Limonene	<0.01–5.2	Aerial parts, flowers, leaves, and twigs	[63,69,70]
Linalool	<0.1–0.4	Flowers, leaves, and twigs	[63]
Longiborneol (=juniperol)	0.3	Flowers, leaves, and twigs	[63]
(E)-β-Ionone	0.6	Flowers, leaves, and twigs	[63]
6-Methyl-5-hepten-2-one	<0.01	Aerial parts and leaves	[69,70]
α-Muurolene	2.2	Leaves	[69]
α-Muurolol	0.1–0.4	Flowers, leaves, and twigs	[63]
γ-Muurolene	<0.01–2.2	Aerial parts, flowers, leaves, and twigs	[63,69,70]
Myrcene	0.2–0.7	Aerial parts, flowers, leaves, and twigs	[63,69,70]
trans-Myrtanol acetate	<0.1–0.2	Flowers, leaves, and twigs	[63]
Myrtenal	0.2–0.3	Flowers, leaves, and twigs	[63]
Myrtenyl acetate	0.4–0.8	Flowers, leaves, and twigs	[69,70]
(*E*)-Nerolidol	0.1	Aerial parts and leaves	[69,70]
Neryl valerate	0.3	Aerial parts and leaves	[69,70]
(E)-2-Nonenal	<0.1	Flowers, leaves, and twigs	[63]
Nonanal	0.3	Flowers, leaves, and twigs	[63]
(Z)-β-Ocimene	<0.01–0.3	Aerial parts, flowers, leaves, and twigs	[63,69,70]
(*E*)-β-Ocimene	<0.01	Aerial parts, flowers, leaves, and twigs	[63,69,70]
1-Octen-3-ol	0.1	Aerial parts and leaves	[69,70]
Palustrol	0.3	Aerial parts and leaves	[69,70]
Patchouli alcohol	4.0	Flowers	[63]
α-Pinene	0.1–8.7	Aerial parts, flowers, leaves, and twigs	[63,69,70]
α-Pinene oxide	<0.01	Aerial parts	[70]
β-Pinene	<0.01–51.3	Aerial parts, flowers, leaves, and twigs	[63,69,70]
cis-Pinocamphone	<0.01–0.3	Flowers, leaves, and twigs	[63]
trans-Pinocarvyl acetate	0.1–0.2	Flowers, leaves, and twigs	[63]
trans-Pinocarveol	<0.01–0.4	Aerial parts, flowers, leaves, and twigs	[63,69,70]
Pinocarvone	<0.1	Flowers, leaves, and twigs	[63]
cis-Sabinene hydrate	<0.01	Flowers, leaves, and twigs	[63]
Safranal	0.1	Flowers, leaves, and twigs	[63]
β-Selinene	0.6	Flowers, leaves, and twigs	[63]

(Contd...)

Table 2: (*Continued*)

Selina-3,7-(11)-diene	0.6	Aerial parts and leaves	[70]
Spathulenol	0.2–2.4	Aerial parts, flowers, leaves, and twigs	[63,69,70]
α-Terpinene	<0.01–3.1	Aerial parts, flowers, leaves, and twigs	[63,69,70]
γ-Terpinene	1.0–1.7	Aerial parts, flowers, leaves, and twigs	[63,69,70]
4-Terpineol	<0.01–0.3	Flowers, leaves, and twigs	[63]
α-Terpineol	<0.01–5.1	Aerial parts, flowers, leaves, and twigs	[63,69,70]
δ-Terpineol	<0.01	Aerial parts and leaves	[69,70]
Terpinolene	<0.01–0.8	Aerial parts, flowers, leaves, and twigs	[63,69,70]
3-Thujanol	0.2	Flowers, leaves, and twigs	[63]
Thymol methyl ether	0.6	Aerial parts and leaves	[69,70]
Tricyclene	0.2	Flowers	[63]
Undecanal	0.1	Flowers, leaves, and twigs	[63]
Valencene	0.2	Flowers, leaves, and twigs	[63]
Valeranone	0.1–2.6	Flowers, leaves, and twigs	[63]
Viridiflorol	0.7–0.9	Aerial parts, flowers, leaves, and twigs	[63,69,70]

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active against *S. aureus* with zone of inhibition of <1.0 mm which was lower than 6.0 mm exhibited by the control. The minimum inhibitory concentration (MIC) values of acetone and methanol extracts against *S. aureus* and *B. cereus* ranged from 312.5 µg/ml to 625 µg/ml, while MIC value of the essential oil against *S. aureus* was 8000 µg/ml which was much higher than MIC values of 0.08–0.31 µg/ml exhibited by the control [69]. Scott *et al*. [62] evaluated the antibacterial activities of the aqueous leaf extracts of *H. petiolare* against *S. aureus, Pseudomonas aeruginosa,* and *Mycobacterium smegmatis* using the disc diffusion assay with ciprofloxacin (50 mg/ml) as a positive control. The extracts exhibited activities against the tested pathogens with zone of inhibition ranging from 9 mm to 15 mm while ciprofloxacin, the positive control exhibited zone of inhibition ranging from 27 mm to 55 mm [62]. Reddy [70] evaluated antibacterial activities of acetone and methanol extracts of aerial parts of *H. petiolare* as well as essential oils isolated from the species against *E. coli, Y. enterocolitica, Klebsiella pneumoniae, S. aureus,* and *B. cereus* using disc diffusion assay with ciprofloxacin (0.01 mg/ml) as a positive control. The extract exhibited activities against *S. aureus* with MIC values ranging from <0.25 mg/ml to 8.0 mg/ml [70]. Similarly, Lourens *et al*. [72] evaluated antibacterial activities of chloroform:methanol (1:1) leaf and stem extracts of *H. petiolare* against *S. aureus, Staphylococcus epidermidis, B. cereus, K. pneumoniae,* and *P. aeruginosa* using the 96-well microplate method with ciprofloxacin as the positive control. The extracts exhibited activities against *B. cereus* with MIC value of 4.0 mg/ml [72].

Antifungal activities

Scott *et al*. [62] evaluated the antifungal activities of the aqueous leaf extracts of *H. petiolare* against *Candida albicans* using the disc diffusion assay with amphotericin (25 mg/ml) as a positive control. The extracts exhibited activities against the tested pathogen with zone of inhibition of 9.0 mm which was comparable to zone of inhibition of 15.0 mm exhibited by amphotericin, the positive control [62].

Antioxidant activities

Lourens *et al*. [69] evaluated the antioxidant activities of acetone and methanol leaf extracts and essential oils of *H. petiolare* using the 2,2-dipheny-l-picrylhydrazyl (DPPH) free radical scavenging assay with ascorbic acid as a reference drug. The extracts showed good DPPH activities with ethanol and methanol extracts exhibiting half maximal inhibitory concentration (IC_{50}) values of 44.3 µg/ml and 28.7 µg/ml, respectively, while the control exhibited IC_{50} value of 2.5 µg/ml [69].

Antityrosinase activities

Sonka [73] evaluated antityrosinase activities of aerial part crude extracts of *H. petiolare* using a tyrosinase assay with kojic acid as a positive control. The extract showed significant effects on tyrosinase with inhibition rate of 44.3% at 50 µg/ml and 59.2% at 200 µg/ml [73]. This study gives some validation toward the use of the species as an antiseptic [11,62] and for the treatment of infections [10,11].

Anti-inflammatory activities

Lourens *et al*. [69] evaluated the anti-inflammatory activities of acetone and methanol leaf extracts and essential oils of *H. petiolare* using the 5-lipoxygenase assay with nordihydroguaiaretic acid as a positive control. The essential oil exhibited activities with IC_{50} value of 25.0 µg/ml while the positive control exhibited IC_{50} value of 5.0 µg/ml [69].

Antigenotoxicity activities

Makhuvele *et al*. [74] evaluated the genotoxicity and antigenotoxicity activities of dichloromethane and 90% methanol leaf extracts of *H. petiolare* against aflatoxin B1-induced mutagenicity using the Ames (*Salmonella typhimurium* strains TA98 and TA100) and Vitotox assays in the presence of S9 rat liver fraction. The extracts exhibited moderate to strong antimutagenic activities in both Ames and Vitotox assays [74]. Such plant extracts with promising antimutagenic effects could be used in the form of feed and food supplements as a preventative strategy against aflatoxin B1-induced mutagenicity and carcinogenicity.

Cytotoxicity activities

Lourens *et al*. [72] evaluated *in vitro* cytotoxicity activities of chloroform:methanol (1:1) leaf and stem extracts of *H. petiolare* against transformed human kidney epithelial (Graham) cells, MCF-7 breast adenocarcinoma, and SF-268 glioblastoma cells at a concentration of 0.1 mg/ml using the sulforhodamine B assay. The extract exhibited Graham cell growth ranging from 33.4% to 76.6% at the tested concentration [72], implying that the species may be toxic against Graham cells.

CONCLUSION

The diverse medicinal applications of *H. petiolare* and the scientific evidence of its biological activities indicate its potential as herbal medicine. There is a need for advanced phytochemical analyses and pharmacological evaluation of the crude extracts as well as compounds isolated from the species aimed at aligning the known medicinal applications of the species with its phytochemistry and pharmacological properties. There is a need for evaluation of the clinical significance of the antioxidant properties, cytotoxicity and toxicity using *in vivo* models.

AUTHOR'S CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICTS OF INTEREST

The author declares that he has no conflicts of interest.

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