PROSPECTS
IN PHARMACEUTICAL SCIENCES

Prospects in Pharmaceutical Sciences, 21(4), 1-9
https://prospects.wum.edu.pl/

Review Article

PAPAVER SPECIES: USAGE AREAS, ESSENTIAL OIL, NUTRIENT AND ELEMENTS CONTENTS, BIOLOGICAL ACTIVITIES

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Received: 20.05.2023 / Accepted: 14.09.2023 / Published: 10.10.2023

ABSTRACT

In this study, the utilisation areas, general characteristics, biological activities, mineral and nutrient contents, and chemical compositions of *Papaver* species were compiled based on literature data. The research findings indicate that *Papaver* species are consumed either directly or in conjunction with other food products. Furthermore, it has been determined that the *Papaver* plant material contains significant amounts of essential nutrients and minerals. Additionally, it has been determined that *Papaver* species may serve as a natural source of antioxidant, antimicrobial, and anticancer compounds. It has been observed that the compounds reported in *Papaver* species may be an important source of many biological activities. As a result, it has been determined that *Papaver* species could be a significant natural resource.

KEYWORDS: antioxidant, antimicrobial, anticancer, medicinal plants, *Papaver*, poppy.

1. Introduction

Numerous natural products are utilised within the scope of traditional and complementary medicine [1]. Since ancient times, people have been utilising natural products to combat illnesses. Traditional medicine, which dates back to earlier times than modern medicine, encompasses the use of various natural products such as fungi, plants, and animals for the treatment or prevention of diseases [2,3]. Throughout history, plants have been utilised by humans for a multitude of purposes including shelter, warmth, sustenance, seasoning, and medicinal applications, among others, as part of the natural product category [4]. It is known that plants that meet the basic nutritional needs of humans are also important natural resources from a medicinal perspective. Numerous researchers across various regions of the world have reported the biological activities of different plant species, such as antioxidant, anticancer, antimicrobial, anti-inflammatory, hepatoprotective, anti-aging, antiallergic, and DNA-protective properties [5-13]. Within this context, the determination of the biological activities of plants is highly significant in terms of identifying their medicinal potentials. In our study, the biological activities, usage areas, general characteristics, mineral and nutrient contents, and chemical compositions of *Papaver* species were compiled based on literature data.

2. Genus *Papaver* and usage areas

The general distribution area of the *Papaver* (family Papaveraceae) genus is the Mediterranean Region. It has been detected in many geographical regions such as the temperate climate zones of Eurasia, Africa, and North America. The genus contains between 70-100 species. The flowers have two sepals that fall off as the bud opens. These petals can be red, pink, orange, yellow, or lilac, with up to four or six petals. The *Papaver* genus comprises annual, biennial, and perennial species that disperse their seeds through wind movements due to their elongated stems [14-17]. It is known that species of *Papaver* are utilised in culinary, ornamental, bakery, tonic, and health-related applications. From a health perspective, it has been determined that the consumption of this plant can be beneficial in cases of measles, headache, rheumatism, cough, insomnia, nervousness, digestive and respiratory disorders, sore throat, cardiac asthma, eye infection, and biliary colic [18-25]. Particularly in the field of healthcare, the contributions of oxycodone, buprenorphine, codeine, and morphine obtained from most species of this genus have been significant in various areas of pharmacology. The authorization procedure for the usage of species belonging to the *Papaver* genus is of great significance.

The use of these plants has been documented due to their active ingredients possessing calming properties. The European Food Safety Authority (EFSA) places significant emphasis on commercial poppy seed status due to its usage reasons. This situation is applicable to decorative objects as well [18-25].

3. Nutritional and elements contents

Plants are an essential component of the human diet. Numerous plant species contribute to human nutrition by either incorporating their various parts into food or by being consumed directly [26]. In our study, we have compiled the nutrient and mineral contents of *Papaver* species reported in the literature. The findings obtained are presented in Table 1.

4. Biological activities

Plants, as natural products, have many biological activities [37]. This study compiles the *in vitro* and *in vivo* biological activity studies reported in the literature for *Papaver* species. Through literature research, it has been noted that various extracts and essential oils of the plant have been utilised, including methanol, ethanol, ethyl acetate, aqueous, hexane, water, petroleum ether, diethyl ether, and chloroform extracts. The findings obtained from the literature review are presented in Table 2.

4.1. Antioxidant activity

All living organisms produce oxidising compounds within their bodies as a result of metabolic activities [66]. Although compounds of this type do not exhibit harmful effects at low levels, they can cause serious damage as their levels increase. Antioxidant defense systems are activated to reduce the harmful effects of oxidant compounds [67,68]. In cases where the antioxidant defence system is insufficient, oxidative stress occurs. Numerous serious illnesses such as multiple sclerosis, cancer, Parkinson's disease, Alzheimer's disease like neurodegenerative diseases may manifest in individuals as a result of oxidative stress [69,70]. Additionally, cardiac

Table 1. Nutritional and elements contents of *Papaver* species [27-36].

	Values	Parts	Values
Protein	3.5-22.16 %	Seeds, leaves	-
Oil	32.43-50.88 %	Seeds, leaves	-
Lipid	45.0-51.2 %	Seeds, leaves	-
Ash	1.9-87.2 %	Seeds, leaves	-
Moisture	3.39-4.76 %	Seeds, leaves	-
Caloric energy (kcal/100 g)	6367.0- 6740.5 %	Seeds, leaves	-
P	0.19-729.0 mg/100g	Seeds, leaves, flowers	17.377-20.099 ppm
K	3.880-521.0 mg/100g	Seeds, leaves, flowers	257.378-287.806 ppm
Na	28.2-960.0 mg/100g	Seeds, leaves, flowers	2.550-5.239 ppm
Fe	4.1-51.7 mg/100g	Seeds, leaves, flowers	0.282-0.293 ppm
Ca	3.60-204.8 mg/100g	Seeds, leaves, flowers	1.60-2.49 ppm
Mg	0.41-511.0 mg/100g	Seeds, leaves, flowers	6.55-7.78 ppm

Table 2. Biological activity of *Papaver* species [38-64].

Plant species	Biological activities	Solvent
***Papaver arenarium* M. Bieb.**	Antioxidant	Methanol
***Papaver bracteatum* Lindl.**	Antioxidant	Methanol
***Papaver decaisnei* Hochst. & Steud. ex Elkan**	Antimicrobial	
***Papaver dubium* L.**	Antioxidant, anticancer	Methanol
***Papaver glaucum* Boiss. & Hausskn.**	Antioxidant	Methanol
***Papaver hybridum* L.**	Antimicrobial	Methanol
***Papaver lacerum* Popov**	Antimicrobial	Ethanol
***Papaver nudicaule* L.**	Antioxidant	Methanol
***Papaver orientale* L.**	Antiinflammatory, antioxidant	Ethanol, ethyl acetate
***Papaver pavoninum* C.A. Mey.**	Antioxidant	Metanol
***Papaver rhoeas* L.**	Cytotoxic, analgesic, allelopathic	Ethanol, aqueous, water
***Papaver somniferum* L.**	Antiinflammatory, antioxidant, antimicrobial, antimutagenic, anticarcinogenic, antiviral, antiproliferative, cytotoxic	Ethanol, ethyl acetate, water, methanol, petroleum ether, diethyl ether, aqueous, chloroform
***Papaver tenuifolium* Boiss. & Hohen.**	Antimicrobial, antioxidant, antiproliferative, cytotoxic	Aqueous, ethanol, hexane, ethyl acetate, methanol, essential oil

disorders may also be observed. Supplementary antioxidants are significant agents in reducing the impact of oxidative stress [71,72]. Plants have a wide range of uses as antioxidant supplements. The *in vitro* antioxidant activity of the methanol extract of the roots, flowers and leaves of *Papaver decaisnei* collected from Iraq was determined using DPPH, ABTS, CUPRAC and FRAP tests. The study reports that the DPPH results ranged from 39.1 to 143.5 µg/mL, the ABTS results ranged from 135.4 to 276.4 µg/mL, the FRAP results ranged from 12.4 to 34.3 µg/mL, and the CUPRAC results ranged from 42.6 to 75.8 µg/mL [40]. It has been reported that extracts of *Papaver rhoeas* collected from Serbia, including ethanol, ethanol-water, methanol, and methanol-water extracts, exhibit inhibition of DPPH free radical scavenging activity ranging from 81.47% to 89.71% [45]. It has been reported that the ethanol extracts and ethyl acetate fractions of *Papaver rhoeas* and *Papaver nudicaule* collected from Kore exhibit high antioxidant potentials as determined by DPPH and nitric oxide scavenging tests [42]. The ethanol-water extracts of various parts of *Papaver rhoeas*, including the root, stem, leaf, and flower, collected from Morocco, were reported for their DPPH free radical scavenging activity and total antioxidant capacity. According to the study findings, the IC50 value of the DPPH test ranged from 0.50 to 2.12 mg/mL, while the results of the total antioxidant capacity test ranged 2.215 -7.014 mg/g [56]. The IC50 value of the antiradical activity of the methanol extract of *Papaver rhoeas* reported from Morocco has been reported as 3.81 mg/mL, and the IC50 value of the maceration extract has been reported as 4.97 mg/mL [53]. It has been reported that the DPPH test of the hexane extract of *P. rhoeas* collected from Bulgaria is 50% [48]. It has been reported that the ethanol extract of *Papaver somniferum* collected from Slovakia has antioxidant activity [58]. In another study conducted in Slovakia, it was reported that *P. somniferum* had antioxidant activity using DPPH, ABTS, FRAP and reducing power tests. In addition, the highest effect was reported to be 146.56 mg/L in the reducing power test [60]. Antioxidant activity of methanol extract of *P. somniferum* collected from Slovakia, Czech Republic, Hungary, and Austria was reported using DPPH and FRAP tests. As a result of the study, it was reported that the highest test results were 337.5 and 488.5 mg/kg, respectively [61]. Antioxidant activity of fixed oil of *P. somniferum* collected from Turkey has been reported using DPPH and ABTS tests. It was reported that the results of the study were 40.35% and 41.09%, respectively [64]. DPPH test results of the methanol extract of root, aerial parts and capsules of *Papaver dubium, P. lacerum, P. arenarium, P. tenuifolium, P. bracteatum* and *P. orientale* collected from Iran varied between 1.22-40.50 mg/g [38]. In a study from Turkey, it was reported that water, ethanol and acetone extracts of *Papaver rhoeas* had antioxidant potentials as determined with lipid peroxidation assay, DPPH assay, reducing power and iron chelation tests [47]. It was reported that the IC50 value of the DPPH test result of the methanol extract of *P. rhoeas* collected from Slovakia was 1.4 mg/mL [46]. It has been reported that the half-maximum effective concentration EC50 value of the water extract of *P. rhoeas* collected from Bosnia and Herzegovina is 28.72 mg/100g as a result of the DPPH test, the FRAP test result is 185.29 mM Fe^{2+}/100 g and the ABTS test result is 12.07 mM TE/100g [49]. In a study from Korea, it has been reported that the ethanol extract of the whole, leaf, and fruit parts of *P. rhoeas* has antioxidant activity in DPPH and ABTS tests [55]. EC50 values of DPPH test result of methanol extract of *P. somniferum* collected from Germany, whole plant, roots, capsule, seed, flowers, stems, leaves and alkaloid extracts were in the range of 7.4-157.6 µg/mL, EC50 values of ABTS test ranged 8.1-306.3 µg/mL and the result of the FRAP test was reported to be 750.1-1348.7 mM $FeSO_4$/g [63]. *P. rhoeas* collected from Poland has been reported to have 71.21% DPPH inhibition [36]. As a result, thanks to the studies, it has been seen that *Papaver* species have a significant effect in terms of antioxidants.

4.2. Antimicrobial activity

In recent years, there has been an observed increase in diseases caused by microorganisms. Antimicrobial drugs are utilised to combat diseases of microbial origin. The increase in the number of resistant microorganisms renders the utilised drugs inadequate [73]. Within this scope, researchers have directed their efforts towards the discovery of novel antimicrobial drugs [74]. In literature studies, the effects of methanol and alkaloid extracts of *Papaver glaucum* and *P. decaisnei* collected from Iraq against *Enterococcus faecalis* and *Pseudomonas aeruginosa* were reported. As a result of the study, it was seen that the MIC value of total tertiary alkaloids of *Papaver decaisnei* against Pseudomonas aeruginosa and *Enterococcus faecalis* was 27.5 µg/mL, and the methanol extract was 200 µg/mL. Additionally, the MIC value of total tertiary alkaloids of *Papaver glaucum* against *Enterococcus faecalis* was 47 µg/mL and of the methanol extract was 180 µg/mL. The MIC of total tertiary alkaloids of *P. glaucum* against *Pseudomonas aeruginosa* was reported to be 47 µg/mL, while the methanol extract was 90 µg/mL [39]. *Papaver hybridum* collected from Turkey, have been reported to have not antimicrobial activity against *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae, P. aeruginosa, Proteus vulgaris, Bacillus cereus, Mycobacterium smegmatis, Listeria monocytogenes, Micrococda lutebuccians, Candida fragilis* strains [41]. It has been reported that the ethanol extract of *Papaver rhoeas* collected from Serbia has different effects against *S. aureus, E. coli, P. aeruginosa* and *Candida albicans* at a concentration of 10 mg/mL. In addition, it was reported that it did not show any effect against *Bacillus subtilis* and *Aspergillus niger* strains in the same study [45]. Extracts of *Papaver rhoeas* collected from Turkey and Northern Cyprus have been reported for anti *Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella pneumoniae, Proteus mirabilis, Escherichia coli, Pseudomonas aeruginosa, Candida albicans* and *Candida parapsisial* activity. As a result of the study, it was reported that the best effect was against *S. aureus* with a MIC value of 1.22 µg/mL and against *C. albicans* with a MIC value of 2.4 µg/mL [51]. It has been reported that ethanol-water mixture extracts of root, stem, leaf and flower parts of *Papaver rhoeas* collected from Morocco have a zone of inhibition of 11.00-13.66 mm against *E. coli, Klebsiella pneumoniae* and *S. aureus* [56]. Methanol extract and macerate of *Papaver rhoeas* from Morocco were reported to be effective between 0.11-60 mg/mL against *Staphylococcus aureus, Listeria monocytogenes, Enterobacter feacalis, Escherichia coli, Klebsiella pneumoniae* and *Salmonella* spp [53]. Inhibition zone values of aqueous extracts of *Papaver somniferum* collected from Pakistan against

Alcaligenes spp, *Citrobacter* spp, *Escherichia coli* and *Micrococcus roseus* were reported to be 8.5, 8.8, 9.5 and 8.1 mm, respectively [57]. It has been reported that the ethanol extract of *Papaver somniferum* collected from Slovakia is effective against *Enterobacteriaceae, Staphylococcus* sp., *Penicillum citrininum, Penicillium crustosum, Penicillium expansum*, *Penicillium brevicompactum* and *Penicillium chrysogenium* [58]. In a study conducted in Turkey, essential oil of *Papaver somniferum* was reported to be effective against *Salmonella typhimurium, Proteus vulgaris, Klepsiella pneumoniae, Bacillus cereus, Bacillus subtilis, Micrococcus luteus* and *Listeria monoaytopenus* [62]. The effects of *Papaver somniferum* collected from Turkey against *Listeria monocytogenes, Enterococcus faecalis, Bacillus subtilis, Staphylococcus aureus, Escherichia coli* and *Salmonella typhimurium* have been reported. As a result of the study, the highest effect was observed against *E. coli* and *L. monocytogenes* [64]. According to literature data, *in vitro* and *in vivo,* studies show that *Papaver* species have significant antimicrobial potential. In this context, it is seen that *Papaver* species can be a natural antimicrobial agent source.

4.3. Anticancer and cytotoxic activity

In this context, it has been reported that the methanol extract of the roots, flowers and leaves of *Papaver decaisnei* collected from Iraq is effective against human colorectal adenocarcinoma (Caco-2), breast cancer cells (MCF-7) and human cervical carcinoma (HeLa) cells. As a result of the study, it has been reported that IC50 values of the flower extracts vary between 223.4-306.5 µg/mL, the leaf parts vary between 165.3-268.2 µg/mL, and the root parts vary between 125.3-388.4 µg/mL [40]. The Brine Shrimp cytotoxic bioassay results of 100 and 1000 µg /mL doses of ethanol extract of *Papaver pavoninum* collected from Pakistan were reported to be 83.3%±1.924% and 96.7%±1.924%, respectively [44]. In a study from Italy, it was reported that the ethanol extract of *Papaver rhoeas* has a high antiproliferative effect on HL60 leukemia human cells [54]. The IC50 values of ethanol extract of *P. rhoeas* collected from Lebanon against cancer cells (HCT116), breast cancer cells (MCF7), human keratinocyte cell line (HaCaT) and non-cancerous colon cells (NCM460) were 160, >200, 110, >200 µM, respectively [52]. The IC50 values of methanol, hexane, ethyl acetate extracts of the root, stem, leaf and capsule parts of *Papaver somniferum* collected from Turkey against HeLa (Human Cervical Carcinoma), HT29 (Human Colorectal Adenocarcinoma), C6 (Rat Brain Tumor Cells) and Vero (African Green Monkey Kidney) cell lines are 113.98-390.64 µg/mL [59]. It has been reported that methanol extract of *P. rhoeas* collected from Slovakia has potent effects against TK6 human lymphoblastoid cell line in the highest used concentration, in lower concentration it has stimulating effect [46]. In a study reported from Korea, ethanol extract of whole, leaf, and fruit parts of *P. rhoeas* was reported to be effective against HepG2 cell lines [55]. It has been reported that alkaloid extracts of *Papaver somniferum* collected from Germany are effective against HeLa, Caco-2, MCF-7, CCRF-CEM and CEM/ADR 5000 [63].

4.4. Anti-inflammatory activity

It has been reported that ethanol extract and ethyl acetate fractions of *P. rhoeas* and *P. nudicaule* collected from Korea have strong anti-inflammatory effects [42]. In another study conducted in Korea, the effect of ethanol extract obtained from *P. nudicaule* sample on RAW264.7 macrophage cells was investigated. As a result of the study, it was found that it was effective in reducing NO induced by lipopolysaccharide (LPS), an important inflammatory mediator it decreased LPS-induced inflammatory cytokines, IL-1ß and IL-6, and inhibited LPS-induced activation of NF-κB and STAT3 [43].

4.5. Other activities

In a study from Pakistan, it was reported that *Papaver pavoninum* had an allelopathic effect on wheat cultivars Ghaznavi and Uqab with added litter and mulching experiments in addition to some extras [43]. Analgesic bioanalysis of ethanol extract of *P. pavoninum* using acetic acid reported that three doses of the extract (50, 100 and 150 mg/kg) were high in acid-induced writhing behavior in mice, but reduced writhing by 36.91%, 57.01% and 68.39%, respectively, at dose reduction [44]. It has been reported that the hexane extract of *P. rhoeas* collected from Bulgaria has antimutagenic and anticarcinogenic properties, since when Zeo is used as an inducer, it reduces Ty1 transposition induced by MMS by 4-5 times [48]. Methanol and ethyl acetate extracts of *P. rhoeas* collected from Korea have been reported to reduce the severity of the cytopathic effects of Influenza in the antiviral activity determined by the Madin-Darby canine kidney cell-based assay [50].

5. Chemical composition

Plants synthesize many biologically active compounds in their own structures. These compounds are known to have many different biological activities [75,76]. In our study, the chemical content of *Papaver* species reported in the literature were compiled. The obtained results are shown in Table 3.

6. Papaver alkaloids

In natural systems, plants face many enemies and therefore have developed multiple defense strategies. As a result of these defense strategies, they produce secondary metabolites [79]. Secondary metabolites have a wide variety of roles. They have many properties such as protection from UV, protection against osmotic and other environmental stresses, attraction of pollinating organisms, allelopathic interactions with other plants, combat against many pathogens and parasites. Also, secondary metabolites play a major role in adapting to the environment against factors such as temperature, drought, humidity, strong light and overcoming stress conditions [80]. Among these secondary metabolites, the most biologically active metabolites are alkaloids. *Papaver* species is a very important source of alkaloids in the plant kingdom. *Papaver* alkaloids, especially berberine and macranthine, have been reported to have significant anticancer activity [81]. They have also been reported to have an analgesic effect [82]. They are widely used in the pharmaceutical industry and food products. The alkaloids found in *Papaver* species are morphine, codeine, thebaine, papaverine, narcotine (noscapine) [83] (Figure 1). Morphine, one of the alkaloids

with strong physiological effects, is often used as

Table 3. Composition of essential oil of *Papaver* species [40,54,62,77,78].

Plant species	Geographic regions	Parts	Essential oil contents
Papaver decaisnei Hochst. & Steud. ex Elkan	Iraq	aerial	roemerine (70.44%), decarbomethoxytabersonine (24.49%), hexadecanoic acid (14-66%-16.40%), 9,12,15-octadecatrien1-ol, (Z,Z,Z)- (12%-25.45%), glycerin(6.41%), 3,4-dihydro-6,7 dimethoxyisoquinoline 2-oxide(5.62%), 2H-pyran-2-one, tetrahydro-4-hydroxy-4-methyl-(4.85%), γ-sitosterol(4.31%-5.31%), benzyl benzoate (3.60%), 8.beta.,13:8.alpha.,14(8.81%), 6,8-dioxa-3-thiabicyclo(3,2,1)octane 3,3-dioxide (8.07%), neophytadiene (4.79), 2-methoxy-4-vinylphenol (4.14%), phytol (3.10%), amitriptylinoxide (3.59%)
Papaver rhoeas L.	Turkey, Italy	aerial	phytol (52.8%), tricosane (7.8%), 2-pentadecanone (6%) , heneicosane (5.3%), dipalmitin (22.30%), 9,12-octadienoic acid (22.50%), 9-octadecenamide, (Z)- (17.15%), 2,6-di-tert-butylphenol (29.95%), elaidic acid (22.15%), hexadecanoic acid (15.90%)
Papaver somniferum L.	Austria, Turkey	aerial, seed	1-Pentanol (3.3–4.9%), 1-hexanal (10.9–30.9%), 1-hexanol (5.3–33.7%), 2-pentylfuran (7.2–10.0%), caproic acid (2.9–11.5%), n-nonadecane (8,96%), heneicosane (10,83%), n-pentacosane (7,91%), n-heptacosane (5,19%), 1-heptacosanol (4,09%), palmitic acid (7,26%), 1-nonadecanol (16,31%)

a narcotic and pain reliever. Codeine is used as a cough suppressant and is less addictive than morphine. Thebaine is the most toxic opium alkaloid and is not used for medical purposes. Papaverine has antispasmodic, diuretic, blood pressure lowering and vasodilating properties. Noscapine is used as a cough suppressant and is not addictive [84]. In this context, medical evaluation of opium alkaloids is thought to be important in the prevention of many diseases.

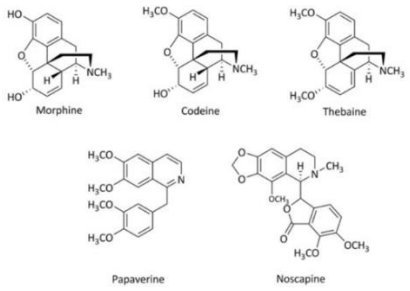

Figure 1. Major opium alkaloids.

7. Conclusions

This study presents a compilation of the general characteristics, usage areas, nutritional and mineral contents, chemical composition, and biological activities of *Papaver* species, based on literature data. The findings of the literature review indicate that *Papaver* species possess significant potential as a source of antioxidants, antimicrobial agents, and anticancer compounds. Furthermore, it has been ascertained that *Papaver* species possess the potential to serve as a natural reservoir of various compounds found within its anatomical structure. Furthermore, it has been noted that *Papaver* species are utilised either independently or in conjunction with comestible items. Within this particular context, it is widely believed that the *Papaver* species holds significant value as a natural resource.

Author Contributions: Conceptualization, F.S.M., I.U., H.H.Y. and M.S.; methodology, F.S.M., I.U., H.H.Y. and M.S.; validation, F.S.M., I.U., H.H.Y. and M.S.; investigation, F.S.M., I.U., H.H.Y. and M.S.; resources, F.S.M., I.U., H.H.Y. and M.S.; data curation, F.S.M., I.U., H.H.Y. and M.S.; writing—original draft preparation, F.S.M., I.U., H.H.Y. and M.S.; writing—review and editing, F.S.M., I.U., H.H.Y. and M.S.; visualization, F.S.M., I.U., H.H.Y. and M.S.; supervision, F.S.M., I.U., H.H.Y. and M.S.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflict of interest.

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