

# Pomegranate Powerhouse : A Synthesis of Scientific Insights into Its Nutraceutical Marvels and Biomedical Applications

Ranjana N<sup>1</sup>, Haripriya S<sup>1</sup>, Mahalakshmi Sundarapandian<sup>1\*</sup>

<sup>1</sup>Division of Biotechnology, JSS School of Life Sciences (Ooty Campus), JSS Academy of Higher Education and Research, Ooty, The Nilgiris, Tamil Nadu, India.

\*Corresponding Author – [mahasundar@jssuni.edu.in](mailto:mahasundar@jssuni.edu.in)

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## ABSTRACT

This comprehensive literature review on pomegranate plants thoroughly examines the various aspects, including traditional uses, nutritional composition, bioactive compounds present in each part of the plant, and their potential activity on human health. The chemical composition of the pomegranate peel and the toxicology of the plant are also discussed. This review also contributes to the understanding of the various pharmacological actions of the pomegranate plant parts. The pharmacological actions of pomegranate include antibacterial activity, antiviral activity, anticancer activity, antioxidant properties, antimicrobial activity, anti-diabetic activity, dermatological activity, and furthermore.

Keywords : Pomegranate, Antimicrobial, Anticancer, Antidiabetic, Dermatology

## I. INTRODUCTION

The Punicaceae family of plants includes the pomegranate (*Punica granatum* L.). Its nutritional and therapeutic qualities make it a significant fruit. Due to their extensive global distribution, pomegranates exhibit a wide range of genetic variations, which lead to variations in their phytochemical makeup (Melgarejo-Sánchez et al., 2021). It is a fruit that is native to the Southeast, the Mediterranean region, Asia, and the United States. It was once thought to have fertility, abundance, and good fortune (Miguel, M. G et al., 2010). The pomegranate tree, also known as the Anar (in Hindi), is a tiny tree or deciduous

shrub that bears fruit and reaches a height of 5 to 8 meters (Fateh et al., 2013). Its fruit can range in color from pale yellow to dark maroon to black and the taste of the fruit can be from extremely sweet to tart like lemons (Preece, J. E et al., 2016). For hundreds of years, the pomegranate, *P. granatum* L., has been used in traditional Chinese and other medical systems, such as Ayurveda, Islamic, and Persian medicine, to treat conditions like diabetes, hypertension, hyperlipidemia, atherosclerosis, and various cancers, as well as oral disorders and peptic ulcers. (Ge, S et al., 2021). Pomegranate consumption may help to enhance gut bacteria, which may help to prevent diabetes and obesity (Chandra et al., 2010).

Pomegranate fruit peel is also used in traditional medicine to treat bronchitis, ischemia, and palpitations. Pomegranate seeds a significant by-product of pomegranate fruit processing, have anti-inflammatory, anti-wrinkle, and anti-diarrheal bioactivities. They can also be used to treat hypercalciuria and glucocorticoid-induced bone loss. Pomegranate bark and leaves have been shown to have positive health effects as well as a variety of pharmacological and therapeutic properties, including antidepressant, antitumor, antibacterial, anti-inflammatory, and antinociceptive effects in a variety of animal species and human disease (Yisimayili, Z et al., 2022). Pomegranates' bioactive components, which include polyphenols, tannins, and anthocyanins, have demonstrated beneficial health effects. The main antioxidant, punicalagin, is widely distributed in the peel of pomegranates.

Pomegranate polyphenols have been found to have a potent antioxidant effect as well as to prevent the growth of pathogenic bacteria, including *S. aureus*, *P. aeruginosa*, *B. cereus*, *E. coli*, and virulence factor, as well as fungi, including *A. ochraceus* and *P. citrinum* (Pirzadeh, M et al., 2021).

#### THE FRUIT:

Pomegranate fruits are berries that are globose or somewhat flattened, 5–12 cm in diameter, and crowned by a thick tubular calyx. The rind, or pericarp, is smooth, coriaceous, and woody, ranging in colour from brownish yellow to red when ripe (Melgarejo et al., 2020). The mesocarp, or albedo, is spongy and divided into several chambers by a horizontal diaphragm and vertical septal membranes composed of papery tissue. The seeds are crammed into each chamber, with many seeds packed on thick, spongy *profundae*; arils not attached to septal membranes (Rana, T. S et al., 2010). The arils, which make up 52% of the fruit's weight and are composed of 22% seeds and 78% juice, are the edible portion of pomegranate fruits. The definition of "Aril" is a tegument linked to the hilum that completely or

partially envelops the seed. Arils are clear, pink, red, or whitish in colour and are separated by membranous walls and white tissue (Valero-Mendoza, A.G et al., 2023).

#### THE FLOWER:

Bisexual, huge (up to 8 cm in diameter), pale red flowers can sometimes be found in clusters of one, two, or even five at the top of the branch. The cup-shaped flower will be fruited, and the bell-shaped flowers typically do not fruit (Ikromovna, T.Z, 2023). Bioactive substances including tannins, terpenes, terpenoids, flavonoids, and organic oils are abundant in flowers (Wafa, B.A et al., 2017 and Wang, D et al., 2018).

#### THE PEEL:

Pomegranate peel, which makes up around 30–40% of the fruit component, is a byproduct of the fruit juice manufacturing industry. The peel is abundant in polyphenols, which include flavonoids, tannins, and phenolic acids, especially anthocyanins.

#### THE BARK:

*P. granatum* bark can grow up to 5 meters tall and is distinguished by its strong, woody brown appearance that appears twisted. The bark of *P. granatum* has long been used to cure a variety of conditions, including ulcers, sore throats, inflammation, and bleeding from the nose (Mashavhathakha, K. L et al., 2014). The bark portion is utilized to treat parasite diseases like malaria (Ge, S et al., 2021).

#### THE LEAVES:

The ovate, green, glossy leaves of *P. granatum* can reach a maximum length of 3 cm and the plant's leaves are perennial or evergreen (Guerrero-Solano, J.A et al., 2020). A different study found that the leaf extract has anti-lice and anti-dandruff qualities, leading to the conclusion that it may be utilized to promote hair development (Bhinge, S. D et al., 2021).

#### THE SEEDS:

The seeds of pomegranate fruit were used to prevent the miscarriage (Moga, M.A et al., 2021). The minimal inhibitory concentration of pomegranate seed ethanolic extracts against streptococcus sanguis was reported (Setiadhi, R et al., 2017).

#### THE FRUIT JUICE:

Pomegranate juice preparations were used to separate polyphenolic substances as punicalagin and punicalin (Fawole, O.A et al., 2016). In addition, the juice has been shown to include calcium, phosphorus, potassium, manganese, zinc, and copper (Guerrero-Solano, J.A et al., 2020).

**BOTANICAL CLASSIFICATION** (Kumari, A. et al., 2012):

Botanical name - *Punica granatum*

Kingdom : Plantae (Angiosperms)

Order : Myrtales

Family : Lythraceae

Genus : *Punica*

Species : *P.granatum*

#### TRADITIONAL USES:

Since ancient times, pomegranates have gained notoriety for their medicinal properties. Pomegranate has been considered the most important drug since Hippocrates, Pliny, Soranus, and Dioscorides wrote about it. Older societies were aware of the pomegranate's health benefits, particularly pomegranate peel extract (Karimi, M et Al., 2017). In Ayurveda, every part of the plant—roots, bark, flowers, fruits, and leaves—is used for medicinal purposes. According to the Ayurvedic medical philosophy, pomegranates are a "pharmacy unto itself". It serves as a blood tonic and an antiparasitic. It cures ulcers, diarrhea, and pharyngitis. In the Middle East and India, the Unani medical system uses pomegranates as a treatment for diabetes (Bhandari, P. R et al., 2012). It was used to treat infertility, inflammation, diarrhea, intestinal worms, and cough in Egypt (Lansky & Newman, 2007). Pomegranate has

also been used to treat snakebites (Jain, S. P et al., 1984).

#### SYNONYMS (Vernacular names)

Hindi : Anar

Sanskrit : Dadimah

English : Pomegranate

Marathi : Dalimba

Gujarati : Dalimba

Tamil : Madulai

Telugu : Danimma

Malayalam : Talimatatalum

Pharsi : Anar tursa

Arabi : Roman Hamiz

German : Granatapfels

Bengali : Dadim

#### POMEGRANATE PEEL CHEMICAL COMPOSITION:

Fresh pomegranate peel powder had a high tannin content and a good nutritional composition, but detanninated peel powder had two benefits: it contained ellagitannin, a separated hydrolysable tannin, and has a good amount of nutritional components and the right amount of tannin, making it a novel supplement for cattle feed (Kushwaha, S. C et al., 2013). The peel extract is used in nutraceutical compositions as physiologically active ingredients, food additives, or functional foods. A good source of bioactive ingredients required for the fruit's biological activity is peel extract, which contains minerals, hydrolyzable tannins (gallic acid), flavonoids (anthocyanins), and phenolic acids (Azmat, F et al., 2024). It was discovered that this powder's higher phenol content and antioxidant activity, along with its good source of crude fiber, offer numerous health benefits, including the ability to lower serum LDL cholesterol levels, improve insulin response and glucose tolerance, lower hyperlipidemia and hypertension, support gastrointestinal health, and prevent certain cancers like colon cancer (Ranjitha, J et al, 2018). Alkaloids, tannins, and dyes can be found

in abundance in the fruit peel, stem (Mirdehghan, S. H et al., 2007).

#### NUTRITIONAL COMPOSITION OF POMEGRANATE PEEL:

Because of their excellent nutritional and chemical makeup, pomegranate peel was employed in a variety of food variations daily (Kandylis et al., 2020). The peel has a high carbohydrate content (59.60%), which is followed by high amounts of moisture (5.40%–5.95%), protein (4.90%–8.97%), ash (3.40%–4.22%), fiber (16.30%–19.41%), and fat (0.85%–1.26%).

#### CHANGES IN FRUIT'S NUTRITIONAL LEVEL DUE TO MATURATION:

The whole seed juice taken from the unripe, half-ripe, and fully ripe stages of pomegranate fruits as well as physical and chemical examinations of the fruit and reported that the fruits became more acidic as they grew more mature, but ripe fruits were much less acidic than green, unripe, and half-ripe fruits (Al-Maiman, S. A et al., 2002). Compared to fructose (46.6%), the percentage of glucose (53.5%) was higher in ripe fruits. Ripe fruits had less polyphenols than unripe ones. Among the other minerals in the fruit, the largest concentrations were found in K, Na, Mg, and Ca. Seeds had higher amounts of Cu, Zn, and Ca, while liquids had higher contents of K, Na, and Fe.

#### BIOACTIVE COMPOUNDS:

Pomegranates have also been found to contain additional bioactive substances such as alkaloids, lignans, proanthocyanidins, xanthonoids, sterols, terpenes, tannins, flavonoids, phenolics, and vitamin C (Maphetu.N et al., 2022).

#### ALKALOIDS:

The main alkaloids found in pomegranate stem and root barks are Pelletierine, Pseudopelletierine, and N-methylpelletierine (Wu, S et al., 2017). The pomegranate fruit extract included low concentrations of alkaloids as well as indolamines,

which are amine derivatives of indole. These include tryptamine, melatonin, and serotonin (Badria, F. A. et al., 2002).

#### ANTHOCYANIN:

Throughout the ripening process, anthocyanins are present in the plant, which is an important bioactive compound giving the colour to the pomegranate (Moga, M.A et al., 2021). The most identified anthocyanins compounds include delphinidin, cyanidin, pelargonidin (Topalović, A et al., 2021).

#### TRITERPENIC ACID:

It was found that various parts of the pomegranate plant contained ursolic acid, one of the chemicals in the triterpenic structure. The leaves and flowers contain 0.45% of the total amount of ursolic acid, whereas the fruit rinds contain 0.6% (Isamuhamedov, A. S., & Akramov, S. T. 1982).

#### TANNIN:

The fruit pomegranate, which is high in polyphenols, has tannins in both its seeds and peels (Jafari, T et al., 2020). The pharmacological characteristics of pomegranates include their direct effects on tannins, which have bioactive components with anti-microbial and anti-viral capabilities (Ko.K et al, 2021). Gallotannins and ellagitannins are two other tannin derivatives that can be discovered in pomegranates (Suručić, R et al., 2021). Castalagin, castalin, casuarinin, corilagin, epicatechin, flavogallonic acid, gallagic acid, gallagylidilacton, granatin A/B, lagerstannin C, pedunculagin, punicalcortin A, B, C, and D, punicalfolin, punicalagin, punicalin  $\alpha$ , and  $\beta$  punicatannin are some of the different isolated tannins from pomegranates (Wang.D et al., 2018).

#### POLYHOLOSIDES:

*P. granatum* contains free oses (SUGARS), water-soluble polyholosides, pectic compounds, hemicellulose A and B, and fructose, glucose, and raffinose in small levels. The polyholoside content of

the fruit rinds was found to be 2.58% (Jurkovic et al, 1976; Keogh and Donovan, 1970).

#### PHENOLICS:

Phenolic substances, including punicalin, gallic acid, ellagic acid, and pyrogallol, were isolated by (Read, E et al., 2019).

#### ELLAGIC ACID:

Among the biological compounds included in pomegranates is ellagic acid (EA), which shows promise as a treatment for a variety of illnesses (Usta, C et al., 2013). Ellagic acid can be found in two different forms: ellagitannins and EA-glycosides (Ismail, T et al., 2012).

#### OTHER COMPOUNDS:

Pomegranate flowers include sitosterol, maslinic acid, asiatic acid, and alkanes (Mohammad, S. M et al., 2012). It was stated that the alcoholic extract included gallic acid, ellagic acid, and D-mannitol (Hartwell, J. L, 1971). Pomegranate juice is said to contain nearly all the amino acids, with exceptionally high concentrations of methionine and valine (Koleva et al, 1981; Konowalchuk and Speirs, 1976). Pomegranate juice was also shown to include protein, riboflavin, vitamin C, thiamin, and inverted sugar (Lad and Frawley, 1986; Malik et al., 2005). Pomegranate seeds have 4 g/kg of estrone (Heftman et al., 1966); its surface portions have 8.7 g/kg, and its blossoms have 2.5 g/kg (Rosenblat et al., 2006; Saxena and Vikram, 2004). Punicic acid, 4-methyl lauric acid, 1,3-dimethyl stearic acid, sterols (stigmasterol, sitosterol), phospholipids (phosphatidyletanolamine, phosphatidylcholine, phosphatidylinositol), as well as mono, di-, and triglycerides and free fatty acids were found when the fatty acid composition of the seeds was examined (Santagati et al., 1984; Sergeeva, 1973).

#### COMPOUNDS PRESENT IN PART OF THE POMEGRANATE:

PEEL: Esteroles,  $\gamma$ -tocopherol and  $\delta$ -tocopherol and  $\alpha$ -tocopherol, punicalagin, flavonoids such as catechin and epicatechin (Elfalleh, W et al, 2011; Muñiz-Márquez et al., 2021).

PEEL AND JUICE: Anthocyanins, delphinidin-3-glucoside, delphinidin-3,5-diglucoside, cyanidin-3-glucoside, cyanidin-3,5-diglucoside, pelargonidin-3-glucoside and pelargonidin-3,5-diglucoside (Fischer, U.A et al., 2011).

SEED AND SEED OIL: Amino acids, nucleosides, phenolic acids, flavones, and coumarins, vitamin E, palmitic, stearic, oleic, linoleic, and punicic acids (Li, G et al, 2020; Tian, Y et al., 2013).

SEED OIL: Steroids, testosterone, b-sitosterol, and campesterol. hydroxybenzoic acids (gallic acid and ellagic acid) and 2 hydroxycinnamic acids (caffeic acid and p-coumaric acid) (Abbasi, H et al, 2008; Eikani, M. H et al., 2012).

#### PHARMACOLOGICAL ACTION:

##### ANTIBACTERIAL ACTIVITY:

Pomegranate extracts shows a strong inhibitory impact against common pathogenic microorganisms, particularly Gram-positive pathogens (Wang, R et al., 2010). Strong inhibitors of *Listeria monocytogenes*, *S. aureus*, *Escherichia coli*, and *Yersinia enterocolitica* were found in the 80% methanolic extract of peels was reported in (Al-Zoreky, N. S et al., 2009).

##### ANTIMICROBIAL PROPERTY:

The antibacterial activity of pomegranate arils and pomegranate juice extracts was determined by several research groups. Commercial pomegranate extract was found to have antibacterial efficacy against *Alicyclobacillus acidoterrestris* spores and vegetative cells (Molva, C et al., 2015).

#### POMEGRANATE ARIL'S PREBIOTIC EFFECT:

Prebiotics are indigestible food additives that can specifically promote the growth and activity of certain gut-beneficial bacteria, most commonly Lactobacillus and Bifidobacteria (Oluwatosin, S. O et al., 2022 & Li et al., 2015) documented the impact of pomegranate juice and extract in their investigation. The findings showed that in vitro stool cultures of both juice and extract strongly suppressed the growth of Clostridia, Bacteroides fragilis, and Enterobacteria while stimulating the growth of Lactobacillus and Bifidobacteria. These results imply that pomegranate manages to work as a prebiotic (Li et al., 2015).

#### ANTICANCER ACTIVITY:

Pomegranate peel has anti-proliferative effects against breast cancer cell lines (Seidi, K et al., 2016). According to (Deng et al., 2017), prostate cancer cells were shown to be inhibited in their proliferation by pomegranate peel extracts, which also caused this form of cancer to undergo apoptosis. Similarly, colon cancer cell lines have demonstrated anti-carcinogenic potential (Gumus et al., 2020; Akhtar et al., 2015; George et al., 2011).

#### ANTIVIRAL ACTIVITY:

Because of the pomegranate's demonstrated antiviral properties, its popularity has been rising (Kharchoufi, S et al., 2018). Gallic acid has been identified as one of the components in pomegranate peel that gives it antiviral qualities. A phenolic component present in fruits and vegetables, particularly pomegranates, is called gallic acid (GA), also referred to as 3,4,5-trihydroxy benzoic acid (Taitzoglou.I.A.et al., 2001). One significant discovery about the antiviral properties of pomegranate peel is its ability to decrease influenza virus RNA replication, which is related to its ability to combat influenza viruses. Punicalagin compounds are the most potent in inhibiting the replication of viral RNA, with an inhibitory effect shown at concentrations as high as 40 mg/mL (Haidari et al., 2009).

#### ANTIULCEROGENIC ACTIVITY:

According to the current study, pomegranate peel extract, particularly sour summer, may have therapeutic benefits as an antiulcer because of its powerful antioxidant content (Ghazaleh, M et al., 2013). The peel of pomegranate shows its antiulcer properties and is advised as a natural treatment for Brexin-induced stomach mucosal damage (Alazzouni, A. S et al., 2021).

#### WOUND HEALING ACTIVITY:

Through a variety of bioactivities, pomegranates are involved in several biochemical pathways and functions throughout the wound-healing process, and they thereby contribute to the healing process in multiple ways. Wound healing is accelerated by pomegranate juice, plant component extracts, and phytochemical treatment (Stefanou, V et al., 2021).

#### ANTIDIABETIC ACTIVITY:

It is reported that type 2 diabetic individuals with hyperlipidemia showed a substantial decrease in their serum levels of total cholesterol and LDL after consuming 40 g/d of concentrated pomegranate juice for eight weeks (Banihani, S et al., 2013). Leaves of pomegranate have antidiabetic properties due to the presence of flavonoids. These flavonoids have the effect of preventing diabetics and their complications (Mohammed, C et al., 2020).

#### ANTIOXIDANT PROPERTY:

Pomegranate juice's ability to scavenge free radicals has been shown in animal experiments. It has also been observed to reduce lipid peroxidation and macrophage oxidative stress. In vitro tests have revealed that pomegranate juice has two to three times the antioxidant capacity of red wine and green tea, while human trials have indicated that pomegranate juice enhances the plasma antioxidant capacity (Gil, M. I et al, 2000; Rosenblat, M et al., 2006; Guo, C et al., 2008). Pomegranate peel extract even increases the hepatic enzymes catalase,



superoxide dismutase, and peroxidase's capacity to scavenge free radicals (Singh, R. P et al., 2002). The overall quantity of phenolic compounds in each cultivar determines its antioxidant activity (Mousavinejad et al., 2009). Interesting antioxidant benefits were demonstrated by a pomegranate peel aqueous extract in a reduced-sugar pomegranate juice jelly (Ventura et al., 2013).

#### DERMATOLOGICAL ACTIVITY:

When taken orally, ellagic acid-rich pomegranate extract inhibits the effects of UV radiation-induced skin pigmentation in humans (Pacheco-Palencia, L. A et al., 2008). Pomegranate extract (PE) from the rind, which contains 90% ellagic acid, was evaluated for its potential to whiten the skin (Bhandari, P. R et al., 2012).

#### ANTINOCICEPTIVE ACTIVITY:

According to a study, pomegranates have active ingredients with antinociceptive and anti-inflammatory properties (Ouachrif, A et al., 2012).

#### ANTI HEMORRHOIDAL ACTIVITY:

Charaka Samiha, a Sanskrit text on Ayurveda, has recommended the internal intake of the decoction of the pomegranate bark and the dried rind to get rid of bleeding piles (Roy, R, 2012).

#### EFFECTS ON MALE REPRODUCTIVE SYSTEM:

Türk et al, (2008) report that when pomegranate juice is consumed, there is a decrease in low-quality sperm and a rise in sperm concentration in the epididymis, as well as increased sperm motility and density.

#### ANTI INFLAMMATORY ACTIVITY:

Pomegranates are one fruit high in polyphenols, and research has indicated that their anti-inflammatory and antioxidant qualities are beneficial to health. Pomegranate has therapeutic effects on chronic inflammatory diseases (CID), with a focus on fruit-derived juices, including inflammatory bowel disease

(IBD), rheumatoid arthritis (RA), metabolic and cardiovascular disorders, and other inflammatory-associated conditions (Danesi, F et al., 2017).

#### EFFECT ON COLON CANCER:

It has been demonstrated that pomegranate phytochemicals prevent colon cancer cells from proliferating and apoptosis (Syed, D. N et al., 2007)

#### ANTIHYPERTENSIVE ACTIVITY:

Daily pomegranate juice consumption for two weeks decreased systolic blood pressure by 5% and the activity of the angiotensin-converting enzyme (ACE) by 36% in hypertension patients (Aviram, M., & Dornfeld, L, 2001). And it was also reported by the short clinical research done, that pomegranate juice lowers hypertension patients' systolic blood pressure and suppresses the serum angiotensin-converting enzyme (ACE) (Yurdasheva, N. P et al., 1978).

#### LIPID METABOLISM REGULATION:

Pomegranate extracts regulate lipid metabolism because they mitigate oxidative stress and the inflammatory response (Hou, C et al., 2019).

#### HYPOGLYCEMIC EFFECT:

On rats given streptozotocin (STZ) to induce diabetes, the hypoglycemic effect of Punica granatum seed extract was reported (Das, A. K et al., 2001).

#### EFFECT ON NEURODEGENERATIVE DISEASE:

Pomegranate extract shows a significant efficacy against neurodegenerative disease including Alzheimer's disease (Mehdi, A et al., 2022).

#### MODERN USE OF POMEGRANATE:

Modern uses of pomegranate-derived products now include treatment of acquired immune deficiency syndrome (AIDS) (Lee and Watson, 2017). Even the peel extract of pomegranate has efficacy against the poliovirus and the Human Immunodeficiency Virus

(HIV) (Stewart, G, 1998) and tumor (Mavlyanov, S et al., 1997).

#### TOXICOLOGY OF POMEGRANATE:

Since pomegranates have been ingested by people for thousands of years, mostly without incident, and in a variety of cultures, they are generally regarded as safe. Nonetheless, some toxicity is known, and there's more out there that needs to be found (Lansky, E. P et al., 2007). Due to the presence of both tannins and alkaloids, consuming the decoction of tree bark and, to a lesser extent, the fruit's pericarps may result in severe acute stomach irritation and even death. No negative effects related to pomegranate consumption, or its components have been documented. Furthermore, no toxicity at levels typically employed in the standard medical system has been reported by animal investigations (Vidal, A et al., 2003). Mild diarrhea is the most common adverse response of pomegranate (Tripathi and Singh, 2000).

#### CONCLUSION:

The study of the literature highlights the potential therapeutic benefits of the pomegranate plant. Pomegranate has anti-inflammatory, anti-cancer, and cardiovascular protective qualities. It is rich in bioactive substances like punicalagins and anthocyanins. According to studies, it may help prevent diseases like diabetes, hypertension, and some types of cancer. Nevertheless, additional clinical trials are necessary to create standardized protocols and dose recommendations for medicinal usage, even though the evidence is encouraging. To sum up, the literature analysis highlights the potential benefits of pomegranates in preventing various diseases and recommends more studies to confirm their use in clinical settings.

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