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Pharmacology, nutrition value and therapeutic potential of honey: A review

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Abstract
Since the dawn of time, honey has been one of the most prized and cherished natural goods available to humans and also being used as a medicine in the traditional medicine systems due to its marvellous medicinal effects in various ailments. It has carbohydrate in the form of glucose, fructose, maltose, sucrose, trisaccharide and other constituents such as water, minerals, proteins, vitamins and enzymes because of the same it serves as a nutritional, preservative and potent therapeutic agent. As mentioned in the Unani system of Medicine, it can be used as nutritive agent and medicinally it has antibacterial, anti-inflammatory, detergent, deobstruent, lithotryptic and wound healing properties. As the bee collects the nectar from flowers to make the honey therefore a significant variation in the properties and looks may occur. Many *in vitro* studies have revealed that it has many pharmacological properties like antibacterial, anti-inflammatory, antioxidant, antiviral, antifungal, and anticancer etc. Present study provides a brief review of medicinal exploration of honey in relation nutrition value, pharmacology, and Therapeutic potential.

Keywords: ASL, Unani medicine, honey, traditional medicine, therapeutic agent

Introduction
Many species of bees, including *Apis mellifera*, *Apis dorsata*, *Apis cerana indica*, *Apis florea*, and *Melipona iridipennis*, produce honey. Generally speaking, honey bees, or *Apis mellifera* bees, gather nectar from flowers and other materials such as fruits and store it in their hive as a very viscous substance with distinct flavour, scent, colour, and texture. Since honey bees gather nectar from a variety of flowers, leaves, and fruits, the nectar has a unique flavour, aroma, and potency. Depending on the habitat, bees gather nectar from poisonous plants also to make honey, which gives honey a strong, spicy flavour [1-3].

History of Honey in Unani
Honey is utilized in the Unani medical system as medicine since a long time to treat various diseases and also used as a base for the preparation of many formulations like *Majeenat*, *Jawarishat* and *Murabbajat*. Use of honey in the formulations also acts as a preservative and nutritive agent [1-2].

The holy scriptures of the Qur'an and the Bible also describe the exploration of honey. Prophet Muhammad (PBUH) was quoted thousands of years ago regarding the importance of honey for people, particularly in the treatment of wound healing and diarrhoea. The father of modern medicine, Hippocrates, treated ulcers, gastrointestinal problems, and wounds using honey. Inspite of this, honey was also given in ancient Rome, either alone or in combination, for conditions relating to the throat, pneumonia, and even snake bites [17-19]. Its colour can be reddish, white, or yellowish, according to Unani literature. It has a reddish color, a wonderful sweet taste, and good viscosity in a wax-free state. Furthermore, as old and faulty honey burns the body's Akhlat (Humors), it might lead to diseases like Junun (melancholia). The classical literature of the Unani states that if we maintain a dead body with honey, it will never deteriorate.

It is mentioned in the Unani classical literature that if we preserve the dead body by applying the Honey it will never be got defected. The fruits and meat can be preserved in it and won't deteriorate for five to six months or three months, respectively, according to Unani literature. [1-2, 4-5].

The first-grade honey's temperate state is dry and hot, whereas the second-grade honey's temperate state is both dry and hot.

In contrast, the ancient honey exhibit was dry in second grade and heated in third. Therefore, it is not recommended for the people bearing the hot and bilious temperament as it produces the excessive thirst, headache and vomiting to them. While by using the honey, people of cold temperament and *Balghami* (plegmatic) diseases get benefitted. On the other hand, the whiter and less viscous honey gradually loses its heat and effectiveness, showing positive effects as a dietary supplement. According to Hakeem Kabiruddin and Hakeem Muhammed Abdul Hakeem if one does not find the honey then he may use the ripen dates in place of honey as a substitute. The ancient honey is assigned to Mars in the Unani medical system, while the sun is said to be related to the stars [1, 3, 5].

Since centuries it has been used as a common sweetener for foods and an effective medicinal agent and as a soothing agent in sore throat [6]. It is frequently eaten as food for the source of energy. Because of the simple carbohydrates it is readily absorbed into the bloodstream [7]. There are a lot of natural products available on the market that are used to cure various illnesses. However, the general public is showing a strong interest in learning more about honey and its products these days.8. Numerous medicinal benefits, including those that are anti-inflammatory, antioxidant, and immune-boosting, are present in honey. Because honey's various medicinal benefits-including its high sugar content, osmotic action, low pH, and ability to produce hydrogen peroxide (H_2O_2)-have been demonstrate [9, 10, 6, 15]. It has highly efficacious ability as a topical medicine in cases of wounds and skin ailments [11]. Local application of Honey to wounds, burns and ulcers enhances the speedy healing by removing infections and rendering the area sterile, encouraging tissue growth and regeneration, and limiting dehydration of the diseased part [12-16].

Composition

Honey is made up of at least 181 different components that revealed its complexity and accomplishment. Honey is reservoir of the sugar's glucose and fructose. Studies revealed that g/100g of the honey consists of Fructose (38.19%), Water (17.20%), Maltose (7.31%), Glucose (31.28%), Higher sugars (1.50%), Free gluconic acid (0.57%), Minerals (0.20%), Proteins (0.30%), Nitrogen (0.04%), Ash (0.17%) and pH value 3.90.

It consists of vitamins such as Niacin, Riboflavin, Thiamine etc. and trace amount of enzymes, melezitose, pentosans, gums and colouring matter also present in honey [8, 20-22, 24, 25].

The dose of honey mentioned in the Unani literature is 22.5-45 grams and most common dose for the same is 24 grams to 60 grams [1, 3, 5, 28, 29].

Table 1: Vernacular name of the honey [23, 28, 31]

Sr. No.	Language	Names
1.	Unani	Mali, Alqolees
2.	Arabic	Asl, Injubin, Asatulnahl,
3.	Persian	Shadab, Angabina, Shahdaan
4.	Sanskrit	Madhu, Makhika, Madhvika, Saragha, Varti, Vanta
5.	English	Honey
6.	Punjabi	Saht
7.	Kashmiri	Mhach
8.	Dutch	Shahad
9.	Hindi	Madhu, Madah, Pehapras, Mehpar, Shahad
10.	Bengali	Mah
11.	Gujrati	Madh
12.	Kannal	Mhou, Tam
13.	Tamil	Mal
14.	Telgu	Taenu
15.	Sindh	Mippany
16.	Burma	Pya-ya
17.	Malyalam	Ayurmader
18.	Turky	Baal
19.	Siryani	Deesa
20.		

Methodology

The material on honey that was available was looked up, gathered, and combined for this article. Using the keywords "Honey" together with other terms like "traditional uses", "medicinal uses", "Therapeutic uses" and "pharmacological activities", a thorough literature search was conducted using Google Scholar, Scopus, Science Direct, and PubMed. In addition, locally and internationally published journals, Unani literature, Unani Books, magazine articles, conference/ seminar proceedings, and pharmacopoeia were also consulted. Using the common database "Plants of the World Online" (Plants of the World Online), a genuine binomial with author citation was confirmed.

Medicinal properties of honey

Honey has been a well-known holistic drug in the world for diseases extending from diarrhoea to inflammation of the eyelids. In Unani system of medicine, it is mentioned as an effective treatment for wounds. From the moderns studies now it has been proved that Honey works better for burns, wounds, and skin ulcers than traditional medical therapies. The Qur'an, the holy book, lists the advantages of honey.

"And thy Lord taught the bee to build its cells in hills, on trees and in (men's) habitations…there issues from within their bodies a drink of varying colours, wherein is healing for mankind. Verily in this is a Sign for those who give thought". In the Surah al-Nahl (the Bee) in Qur'an [26]. Prophet Muhammad (PBUH) highly suggests honey for therapeutic purposes [27].

Table 2: Pharmacological actions of the honey in relation to Unani Medicine

Sr. No.	Unani term	English equivalent	Reference
1.	*Muhallil-e-Waram*	Anti-inflammatory	[1, 3, 5, 28, 31]
2.	*Musakkin-e-Auja'a*	Pain killer	[1, 3, 5]
3.	*Mughazzi*	Nutrient	[1, 5, 28]
4.	*Jali*	Detergent	[1, 3, 5, 28, 30, 31]
5.	*MufattehSudad*	Deobstruent	[1, 3, 28]
6.	*Mufattehafwahuruq*	Vasodilator	[28]
7.	*Mufattit e Hisa't*	Lithotryptic	[1, 3, 28]
8.	*Muqawwi e Mida*	Tonic for stomach	[1, 3, 28, 31]
9.	*Mushtahi*	Appetizer	[1, 3, 5, 28, 31]
10.	*Muqawwi e Bah*	Aphrodisiac	[1, 3, 5, 28, 29]
11.	*Daf e Taffun*	Antiseptic	[1, 3, 5, 28, 31]
12.	*Hadim*	Digestive	[1, 3, 5, 31]
13.	*Munaffith e Balgham*	Expectorant	[1, 3, 5, 28]
14.	*Musaffi e Dam*	Blood purifier	[1, 5, 28]
15.	*Mundamil-e-Qurooh*	Wounds Healer	[1, 3, 5]
16.	*Muqawwi e basar*	Eye tonic	[1, 3, 30]
17.	*Munqi e dimagh*	Brain cleanser	[1, 3, 28]
18.	*Muqawwi e dimagh*	Brain tonic	[1, 3, 28]
19.	*Muqawwi e dandan*	Tooth Tonic	[1, 28]
20.	*Mudirr-i-Laban*	Galactagogue	[1, 28]
21.	*Mudirr e baul*	Diuretic	[1, 28]
22.	*Mudirr e haiz*	Emmenagogue	[1, 28]
23.	*Musakhin*	Tranquilizer	[28]
24.	*Mujaffif*	Desiccant	[28]
25.	*Mulayyin*	Laxative	[28]

Table 3: Therapeutic uses of honey in relation to the Unani medicine.

Sr. No.	Unani term	English equivalent	Reference
1.	*Istisqa*	Ascites	[1, 3, 28]
2.	*Qillat al baul*	Oligouria	[1, 28]
3.	*Laqwa*	Bell's palsy	[1, 3, 5]
4.	*Falij*	Paraplegia	[1, 3, 5, 28, 29]
5.	*Istirkha*	Atony/flaccidity	[1, 3, 28]
6.	*Sual e Balghami*	Productive cough	[1, 3, 5, 28]
7.	*Khidr*	Numbness	[1, 28]
8.	*Qulanj*	Colic	[28]
9.	*Dast*	Diarrhoea	[1, 28]
10.	*Nazul al maa*	Cataract	[1, 5, 28]
11.	*Zarabwahikka*	Pururitis	[28]
12.	*Damaa*	Epiphora	[1, 5, 28]
13.	*Bayaz*	Corneal opacity	[1, 28]
14.	*Sayalan al-Udhun*	Otorrhoea	[1, 5, 28]
15.	*Sakl e samaat*	Deafness	[28]
16.	*Taneen*	Tinnitus	[1, 28, 29]
17.	*Waja al Uzn*	Earache	[1, 5, 29]
18.	*Qurooh*	Wounds	[1, 3, 5, 28, 31]
19.	*Qurooh e amaa*	Intestinal ulcer	[28]
20.	*Kalaf*	Chloasma	[1, 3, 28, 29]
21.	*Bahaq*	Pityriasis	[28]
22.	*Baras*	Vitiligo	[28]
23.	Quba/Daad	Ring worm/dermatophytosis	[1, 3, 28, 29]
24.	*Waram e Lauzatain*	Tonsillitis	[1, 3]
25.	*Kuttekakaatna*	Dog bite	[1, 28]
26.	*Yaraqan*	Jaundice	[1, 3, 28]
27.	*Azm e Tihal*	Enlargement of spleen	[1, 3, 28]
28.	Khushunat e Halaq	Sore throat	[1]
29.	*Amraz e Ria*	Chest diseases	[1, 5, 28]
30.	*Du' ƒ al Bah*	sexual debility	[1, 3, 28]
31.	*Hisat e Kuliya*	Renal calculi	[1, 3, 28]
32.	*Deedan e Ama*	Intestinal worms	[1, 28]
33.	*Qabz*	Constipation	[1, 5, 28, 29]
34.	*Usr-al baul*	Dysuria	[1, 3, 28]
35.	*Amraz e raham*	Uterine diseases	[1, 3, 28]
36.	*Irqunnisha*	Sciatica	[1, 28]
37.	*Aqrabghazidgi*	Scorpion bite	[28]

Table 4: Physico-chemical Properties/Constituent of honey [32, 33, 34, 35, 36, 37].

Sr. No.	Properties	Characteristics
1.	Colour	Yellow to brown ranges from clear and colourless (like water) and dark amber or black.
2.	Taste	Sweet, faintly acrid
3.	Moisture content	18-23%
4.	PH value	3.2-4.5
5.	Electric conductivity	0.22-1.52 $mScm^{-1}$
6.	Ash value	0.14-0.30%
7.	Insoluble matter	0.12-0.5%
8.	Hydroxyl methyl furfural	<40 $mgkg^{-1}$
9.	Proline	>180 $mgkg^{-1}$
10.	Total acidity	<40 $meqkg^{-1}$
11.	Thermal conductivity	118-143x10Cal/cm^2/ oC13
12.	Lipids	0.37-0.39%
13.	Fat	0 g / 100 g
14.	Protein	0.5 g / 100 g
15.	Calcium	4-30 mg / 100 g
16.	Chlorine	2-20 mg / 100 g
17.	Copper	0.01-0.1 mg / 100 g
18.	Iron	1-3.4 mg / 100 g
19.	Magnesium	0.7-13 mg/100 g
20.	Phosphorus	2-60 mg/100 g
21.	Potassium	10-470 mg/100 g
22.	Sodium	0.6-40 mg/100 g
23.	Zinc	0.2-0.5 mg/100 g
24.	Manganese	0.02-2 mg/100 g
25.	Chromium	0.01-0.3 mg/100 g
26.	Selenium	0.002-0.01 mg/100 g
27.	Invertase activity	178.78-187.7 unit/kg
28.	Diastase number	22.5-44.77
29.	Vitamin B1(Thiamine)	0.00-0.01 mg/100 g
30.	Vitamin B2(Riboflavin)	0.01-0.02 mg/100 g
31.	Vitamin K (Phylloquinone)	ca.0.025 mg/100 g
32.	Vitamin B6(Pyridoxin)	0.01-0.32 mg/100 g
33.	Ascorbic acid	2.2-2.5 mg/100 g
34.	Niacin[2]	0.10-0.20 mg/100 g
35.	Pantothenic acid	0.02-0.11 mg/100 g

Pharmacology of honey

1. **Anti-inflammatory activity** [38-42, 48, 49]
   It is mentioned in the Unani classical literature that honey is very effective anti-inflammatory drug used to treat inflammation. Whereas in the modern era it has been reported that honey showed its anti-inflammatory activity by lessening the activities of COX-1 and COX-2. In addition, in the plasma of individuals bearing the normal state of health, some prostaglandins (PGE2, PGF2α and thromboxane B2) were found reduced on consuming the natural diluted honey. On the other hand, the activation of NF-κB is widely recognized as a vital factor in the pathogenesis of inflammation. Whereas, some recent studies also reported that Gelam honey inhibits the activation of NF-κB pathway.

2. **Anti-atherosclerosis and prevention from cardiovascular diseases** [43-46]
   Honey from different sources may contain the flavonoids like acacetin, apigenin, catechin, chrysin, galangin, hesperitin, kaempferol, luteolin, myricetin, naringenin, naringin, quercetin, rutin, and many of them act as very potent therapeutic agents. Like on the development of atherogenic alteration of Low-Density Lipids and aortic atherosclerotic plaques, inhibitory effect of catechin, naringin and quercetin have been mentioned in reports. The findings of the researches have suggested that by increasing NO production in human endothelial cells, rutin may enhance endothelial function. According to reports, flavonoids may play a role in preventing cardiovascular disease primarily through reducing oxidative stress and raising the bioavailability of nitric oxide (NO).

3. **Anticataract activity** [47]
   The *in vitro* synthetic flavonoids orientin, luteolin 3'-7-diglucoside, and luteolin 4'-glucoside significantly reduced the development of cataracts in ovine lenses cultured in 45% hypotonic HBS for a full day. It could be viewed as preliminary proof of stingless bee honey's potential anti-cataract qualities.

4. **Anti-oxidant activity** [50-52]
   In a recent study on 90 samples of honey was explored for, photo chemiluminescence techniques were used to examine the antioxidant capacity of honeys. The DPPH and FRAP methods were applied as the reference. The Folin-Ciocalteu method was used to calculate the total phenolic content (TPC). Regardless of the method employed, buckwheat was found to have the strongest antioxidant activity, while rape honeys had the lowest. Another study done on the buckwheat honey indicated that elevated plasma antioxidant and total phenolic content were observed after the use of honey at the dose of 1.5g/kg body weight.

5. **Prevention of gingivitis and dental caries** [53]
   A randomized controlled study done by Al-Dany it was reported that after orthodontic treatment, honey can be

used instead of conventional treatments to prevent dental caries and gingivitis.

6. **Anti-Microbial activity** [54, 56]
In the back of this property of honey many biochemical qualities and biological activities such as the acid content of honey, water activity, osmotic pressure, presence of bioactive compounds like phenolic acids, defensin-1, flavonoids, hydrogen peroxide (H_2O_2), lysozyme, methylglyoxal (MGO), volatile compounds as well as antibacterial products secreted from the lactic bacteria, plays their major role. In fact, biological activities of primitively cumulated floral source, season, geographical emanation, honey age, health of bees, storage conditions and suitable beekeeping practices decides the inbred anti-microbial potential of honey. Abdelhadi Hbibi in his review also concluded that honey has significant anti-microbial property.

7. **Antivirals** [55, 57]
An *in vitro* study conducted on the manuka and clover honey revealed the anti-viral activity on varicella-zoster virus. In another study results revealed the potent inhibitory property against the influenza virus.

8. **Antifungal activity** [58]
During the *in-vitro* study on four types of honey from Western Algeria observed that the honey samples bear the antifungal property against *Rhodotorula* sp. and *Candida albicans.*

9. **Anti-tussive activity** [59-61]
Hibatullah Abuelgasim stated that honey is much better to usual care for the betterment of symptoms like cough frequency and cough severity of upper respiratory infections. Olabisi Oduwole in his review concluded that when compared to diphenhydramine, placebo, and no treatment, honeys likely reduce cough symptoms more than other options, although it might not have much of an impact when compared to dextromethorphan. S.M Sopo advocated that findings of their study and evaluation of the literature suggest that milk and honey are at least as effective as over the counter cough treatments for the treatment of non-specific acute cough in children.

10. **Wound and Ulcer healing activity** [62-66]
Ahmad Oryan and Hana Scepankovain in the report mentioned that the wound healing property of honey is due to its hydrogen peroxide, acidity, high osmolality, nitric oxide, phenols and non-peroxide factors. Honey speeds the healing of wounds by encouraging autolytic debridement, promoting the development of wound tissues, and stimulating anti-inflammatory actions. Honey also provides the protection from the microbes and reduces the wound area by enhancing the re-epithelialization therefore it is more efficacious then other topical agents used for the wound healing. In a pilot study on 10 patients, 80% pain was relieved on 15th day, on 15th day in 80% cases tenderness was reduced, in 50% of the cases on 7th day healthy granulation developed while burning sensation and discoloration around the wounds were significantly remitted on 7th day. So, the honey found to be very effective and economical dressing material in comparison to others. The data in the review by Noori S. Al-Waili revealed that honey can used to treat chronic wounds, ulcers and burns.

11. **Anti-Diabetic Activity** [67-69]
In the study various honeys of raw and processed form prepared by different bees to assess the therapeutic effect were taken. Alpha glycosidase and alpha amylase *in vitro* enzyme inhibition assays were the two methods utilized to determine the anti-diabetic potential of honeys. Trigona honeys demonstrated the highest percentage of inhibition against alpha amylase and alpha glucosidase enzymes, respectively, out of all the honeys tested in two distinct ways, at 500 µg/ml, raw (77.61% & 80.46%) and processed (64.84% & 78.29%). Additionally, analysis showed that honeys had moderate glycemic index and glycemic load levels. This makes its occasional use possible for diabetics.
The normal group, the diabetic control group, the diabetic group treated with conventional glebenclamide, the diabetic group treated with 200 mg/kg of bitter honey, and the diabetic group treated with 400 mg/kg of b.w. honey were the subjects of another investigation. Nicotinamide and streptozotocin increased the risk of type II diabetes Wistar Albino The anti-diabetic action was carried out on rats. The diabetic rats who were given bitter honey treatment, their fasting blood glucose levels were significantly lower (p<0.05) than the rats were not given any treatment.

12. **Haemostasis property** [70, 71]
The inhibitory effect on the blood coagulation and platelets aggregation was described by the study done by Ahmed, *et al.* 2011. These findings give the preliminary evidence on the modulatory role(s) of honey on haemostasis process. In a review it is mentioned that honey bears the anti-platelet potential due to its phenolic compounds.

13. **Angiogenic property** [72, 73]
A study was carried out by R. M. Munshi to evaluate the angiogenic property of the honey on vascular endothelial growth factor expression in the Chick Chorioallantoic Membrane CAM tissue. The results revealed that honey bears the pro-angiogenic potential at low concentrations. In another study positive results for the angiogenesis were found positive which were validated by using the Angiokit system.

14. **Anti-proliferative and apoptotic property** [74, 75, 76]
The antiproliferative and apoptotic effects of honeys from Spain were recognized by chromatin condensation and flow cytometry analysis. Apoptosis was induced in HL-60 cells very effectively by the polyfloral, heather containing the higher phenolic honeys. Another study advocated about the chrysin flavon present in the honey that it may be the responsible potent compound for the prevention and treating the Prostate cancer. A literature review data also supports the anti-proliferative and apoptotic activity of the honey.

15. **Anti-mutagenic Activity** [77, 78]
The Ames experiment was used to evaluate the anti-mutagenic properties of different honeys, and the results showed that all honeys significantly suppressed Trp-p-1, a food mutagen that is known to be carcinogenic in

animals and mutagenic in bacteria. By using the same tool another study concluded that honey samples have good anti-mutagenic effect.

16. **Effect of honey on gastritis, gastroenteritis, gastric and duodenal ulcer** [79]
In a study it was observed that all honeys samples were found to have the antibacterial activity specially against the *H. Pylori*. It was also suggested that the use of honey with triple therapy regimen will decrease the duration of treatment of gastritis or duodenal ulcer patients infected by the *H. pylori*.

17. **Used in Arthritis** [80]
A study was carried out in female Wistar rats with MIA-induced osteoarthritis, revealed that the honey in low dose and then in high dose was more effective in reversing the course of the illness and generating anti-inflammatory and antinociceptive effects.

18. **Antibacterial activity** [81-83]
Using the agar dilution method anti-bacterial activity of Medihoney and Manuka was assessed against bacteria and yeast at five concentrations varying from 0.1 to 20% found to be very effective. According to a study, *S. aureus* was the most sensitive microbe to the antibacterial activity of honey extracts, whereas *B. subtilis*, *S. lentus*, *K. pneumoniae*, and *E. coli* were all reasonably susceptible. In both its crude and diluted forms, honey's anti-microbial activity was evaluated against *Pseudomonas aeruginosa*, *Shigella dysenteriae*, *Salmonella typhi*, and *Staphylococcus aureus*. The findings showed that when it came to the test pathogens, crude honey had a higher level of antibacterial activity.

19. **Immuno-modulatory activity** [84]
A study suggested that honey has the immunomodulatory potency and can improve the carbon tetrachloride induced immune disease in rats through adjusting the quantities of TNF-α, IFN-γ, and other inflammatory cytokines.

20. **Poisonous Honey**
There have been cases of humans being harmed by a certain type of honey's deadly effects documented in previous numerous reports. This is because when honeybees gather nectar from poisonous plants like *Rhododendron* sp., *Coriaria arborea*, and *Tripterygium wilfordii* Hook F., food safety concerns for honey develop. Toxic honey consumption can cause euphoria signs in humans and can even be lethal in certain situations. This may be the cause of dizziness, nausea and vomiting and that may be due to the plant_toxins such as pyrrolizidine alkaloids, triptolides, tutin and grayanotoxins, in the toxic honey.

Conclusion
Honey is a very potent remedy used in Unani System of Medicine since long-long ago orally and locally. It has many reassuring properties of Anti-inflammatory, Anti-oxidant, Angiogenic, Antimicrobial, Anti-tussive, Wound and Ulcer healing activity and many more. As it is a time-tested medicine used in traditional systems but the documentation is lacking. This is a need of the hour that its activities should be evaluated further by the researchers for the properties as mentioned in the Unani System of Medicine. If we achieve the goal this will be a great achievement for the mankind.

Declaration of conflict of interest
We have no conflict of interest to declare.

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