

Fruit power: pomegranate helps fight Hepatitis C infection

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Hepatitis C affects more than 170 million people worldwide causing liver cirrhosis and cancer¹. It is an infectious liver disease caused by the Hepatitis C virus (HCV) that is known to infect only humans and chimpanzees. It gets transferred from person to person through blood contact mostly due to improper sterilization methods or blood transfusion. According to the April 2014 reports of the World Health Organization (WHO), the regions with the highest HCV patient count are South and East Asia (100 million) and North and Central Africa (15 million)¹. In India, more than 12 million people suffer from highly chronic form of Hepatitis C. It is a fast emerging threat to public health however, there are very few effective preventive programmes aimed at spreading awareness about Hepatitis C infection. Treatment though available, is very expensive with less than 50% chance of cure². The existing treatment for Hepatitis C is a combination of an antiviral drug, ribavirin and an immune-system modulator called interferon. The treatment extending for about 24 to 48 weeks costs about Rs 375,000, making it unaffordable to the economically weaker sections of the society. However, as far as we are aware, unlike in the cases of HIV and TB, treatment for Hepatitis C is not available at subsidized rates. Recently Gilead Sciences, a pharmaceutical company based in the USA announced that it would introduce in India, the drug 'Sovaldi', a 12-week treatment course used for treating Hepatitis C infection costing 99% cheaper than its price in



Pomegranate (*Punica granatum*) is known for its many medicinal properties. Photo: en.wikipedia.org.

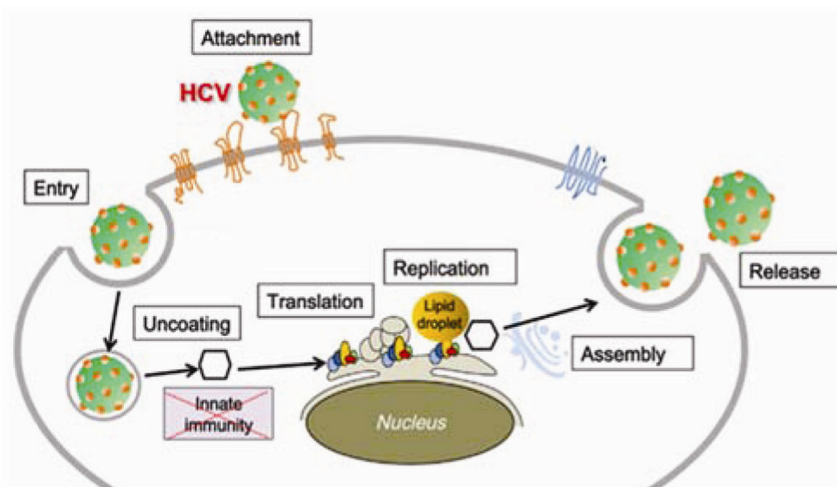
the USA. Even at such high discounted rates, the drug would still cost US\$ 900 or Rs 54,000 (ref. 3). However, apart from being expensive, these treatments come with many side effects like nausea, anaemia, fatigue and depression in some extreme cases.

In a breakthrough discovery, scientists from the Indian Institute of Science (IISc), Bangalore have found that bioactive compounds from the pomegranate fruit not only help prevent Hepatitis C infection but also fight it⁴. The research team led by Saumitra Das of the Department of Microbiology and Cell Biology, has been working on the translation and replication mechanisms of HCV for many years now.

HCV is an enveloped, positive-sense RNA virus. Once inside the human body it is able to recognize the liver cells that are specialized in their function and have unique protein receptors present on the cell surface which help the HCV to adhere to the cells and slowly enter it. Once virus enters inside the liver cell, its envelope is dissolved resulting in uncoating of the RNA genome. The uncoated RNA now produces viral proteins that weaken the cell's immunity and the virus begins to replicate within the cell, using the cell's resource and assembles new viral RNA strands coated with protein envelopes. These new viruses are then released outside the cell, where they infect

the neighbouring cells and continue the process all over again.

After a review of the literature on plant-based substances that are known to have hepato (liver) protective and antiviral properties, the research team narrowed down on pomegranate (*Punica granatum*). Pomegranate is known to have many medicinal properties. The bark of the pomegranate tree, the fruit peel and the fruit are widely used in Ayurveda to cure stomach ailments and blood disorders like anaemia. Previous research has indicated that pomegranate being rich in flavonoids and antioxidants, helps in preventing cancer and Alzheimer's disease⁵. The pomegranate fruit peel contains punicalin, punicalagin and ellagic acid; bioactive compounds that inhibit the activity of the NS3 enzyme of HCV. The NS3 is a non-structural protein of HCV, which helps in polyprotein processing and replication of the viral RNA, within the host cell. By inhibiting the activity of NS3, the three compounds were found to be successful in stopping further replication of the virus. A series of tests were conducted to study the three compounds for their anti-HCV properties. A culture of liver cells was treated separately with punicalin, punicalagin and ellagic acid. They were then infected with HCV. It was observed that the treated cells stopped HCV from entering them. In cells that were already



Life cycle of HCV in a human liver cell. Photo: <http://journal.frontiersin.org>.

infected by HCV and then treated separately with the three compounds, it was observed that the replication of the virus within the cell was significantly reduced. The three compounds, punicalin, punicalagin and ellagic acid were then compared with the drug Telaprevir, which is commercially available and used in the treatment of Hepatitis C. All three compounds, when tested in high doses had similar level of effectiveness on inhibiting the activity of NS3 as that of Telaprevir.

The drugs presently prescribed to treat Hepatitis C are associated with several side effects. Therefore, the three compounds were experimentally tested to investigate whether they would have any negative effects on the normal function-

ing of the liver cells. It was observed that the three compounds inhibit virus without any toxicity to the host cells. To further confirm the same, high doses of the three compounds were separately administered to laboratory mice and their livers were examined for signs of toxicity. The result showed that these compounds were tolerated well. Another interesting observation found in this study was that these compounds were also readily available in the blood stream of mice, for absorption by the liver cells. The researchers are now conducting more experimental tests to confirm the effectiveness of the three compounds isolated from pomegranate, in preventing Hepatitis C infection and to help develop a drug that is cheaper and safer for treating the infection.

1. Guidelines for Screening and Treatment of Persons with Hepatitis C infection. WHO Report, 2014.
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