

Grapefruit Juice: Nutritional Values and Drug Interactions

Sujit Kumar Sarker ^{*1}, Khin Darli Tun ¹, Eliza Omar Eva ², Ratna Paul ³.

^{*1} Faculty of Medicine, International Medical School, Management & Science University, Shah Alam, Selangor, Malaysia.

² Department of Pharmacology, Dhaka Medical College, Dhaka, Bangladesh.

³ Mohammadpur Fertility Services & Training Centre, Mohammadpur, Dhaka, Bangladesh.

ABSTRACT

Introduction: Grapefruits are large, rounded citrus fruit. The fruits were bred in 18th century as a cross between pomelo and orange. They were given the name grapefruit because of the way they grew in clusters similar to grapes. Grapefruits vary from yellow to pink and red. Its taste also varies from sour or bitter to sweet. Its flesh is either pink or white colour.

Nutritional values: Grapefruits are low in calories but full of nutrients. It provides calories, niacin, ascorbic acid, vitamin A, potassium, phosphorus, calcium, carbohydrate, protein, fat, iron, sodium, riboflavin and thiamine. Grapefruit juice help to lower risk from many diseases and also help to reduce weight.

Pharmacology: Certain substances in grapefruit juice inhibit the cytochrome P450 (CYP3A4) and increase plasma concentrations of co-administered drug that can produce toxic effect. Grapefruit juice also lower plasma drug concentrations with few drugs by inhibiting drug absorption catalysed by the organic anion transporting polypeptide (OATP). By inhibition of P-glycoprotein grapefruit juice also increases bioavailability of oral drug.

Drug interactions: The opportunity for a food-drug interaction is common for grapefruit juice. It has potential interactions with lipid lowering agents, calcium channel blockers, cytotoxic drugs, antidepressants, antimalarials, drugs used in erectile dysfunction and many other drugs as well.

Conclusion: As Grapefruits have potential interactions with many medicines so it should be taken cautiously and further research are required for optimal use.

KEY WORDS: Grapefruit, Grapefruit juice, Food-Drug interactions, Citrus fruit interactions.

Address for correspondence: Dr. Sujit Kumar Sarker, Department of Pharmacology, Faculty of Medicine, International Medical School, Management & Science University, Malaysia,
E-Mail: sujit_swapna@yahoo.com

Online Access and Article Information

Quick Response code



DOI: 10.16965/ijims.2015.134

International Journal of Integrative Medical Sciences

www.imedsciences.com

Received: 18-10-2015

Accepted: 02-11-2015

Reviewed: 19-10-2015

Published: 10-11-2015

Source of Funding: Self

Conflicts of interest: None

INTRODUCTION

Grapefruit is generally accepted as *Citrus X paradisi* which is a hybrid between pomelo and orange. The fruit was first described in 1750 by Griffith Hughes and in 1789, Patrick Browne reported it as growing in most parts of Jamaica and he referred to it as "forbidden fruit" or "smaller shaddock". Grapefruits grow in warm subtropical climate. Temperature and humidity

differences affect the length of time from flowering to fruit maturity and peel thickness. The tree has a rounded top of spreading branches and the green leaves are ovate and dotted with tiny oil glands. The white, 4-petalled flowers, borne singly or in clusters in the leaf axils. The fruit is nearly round or slightly pear-shaped, 10-15 cm wide with smooth, finely dotted peel, up to 1 cm thick and aromatic

Fig. 1: a. Fruit b. Flower c. Tree of Grapefruit [13].



outwardly. The center may be solid or semi-hollow. The pulp is yellow or pink to red, which has 11 to 14 segments with thin membrane. The fruit is very juicy and acid to sweet-acid in flavor. The fruit present with pointed seeds about 1.25 cm in length and seedless variety is also available. Grapefruit seeds are usually polyembryonic and the number of fruits in a cluster varies greatly [1].

NUTRITIONAL VALUES

In 1970, grapefruit diet plan was promoted widely to achieve a loss of 10 lbs weight in 10 days. The fruit is customarily a breakfast fruit. Some consumers sweeten it with sugar or honey. Some add cinnamon, nutmeg or cloves. It is also served as an appetizer before dinner. The sections are commonly used in fruit salads, puddings and tarts. It is also processed as marmalade in Australia. The juice is marketed as beverage. It also can be made into an excellent vinegar or carefully fermented as wine. Raw grapefruit juice (per 100gm) contain calories 37-42, moisture 89.2-90.4g, niacin 0.2mg, ascorbic acid 36-40mg, vitamin A 10-440 IU, potassium 162mg, phosphorus 15mg, calcium 9mg, carbohydrate 8.8-10.2g, protein 0.4-0.5g, fat 0.1g, iron 0.2mg, sodium 1.0mg, riboflavin 0.02mg, thiamine 0.04mg [1].

PHARMACOLOGY

Grapefruit have been demonstrated to have a preventive influence on many chronic diseases, such as cancer and cardiovascular diseases [2]. An essence prepared from the flowers is taken to overcome insomnia, also as a stomachic and cardiac tonic. The pulp is considered an effective aid in the treatment of urinary disorders. Leaf extractions have shown antibiotic activity [1]. However, since the early 1990s, the potential health benefits of grapefruit have been oversha

-dowed by the possible risk of interactions between drugs and grapefruit juice [2]. Concomitant administration of grapefruit juice can increase the plasma concentration of numerous drugs in humans and also decrease the concentration of few other drugs [3].

Grapefruit juice can alter oral drug pharmacokinetics by different mechanisms. Relevant mechanisms include modulation of the activity of cytochrome P450 (CYP) 3A, organic anion transporting polypeptide (OATP) and P-glycoprotein [3-7].

Increased concentrations of co-administered drugs are mainly mediated by chemicals in grapefruit juice that inhibit the CYP 3A4 drug-metabolizing enzyme in the small intestine. This inhibition decreases the first-pass metabolism of drugs using the CYP 3A4 enzyme system and increases the bioavailability and plasma drug concentrations. The effect of grapefruit juice on drug metabolism is most pronounced in drugs with a high first-pass metabolism [3].

Organic anion transporting polypeptides (OATPs) are a group of membrane transport proteins that present in enterocytes, which facilitate the gastrointestinal absorption of certain orally administered drugs. OATP-inhibiting substances are likely to be present in higher concentrations in many commercial fruit juices [8]. The use of grapefruit juice with a few drugs may lower plasma drug concentrations by inhibiting drug absorption catalysed by the organic anion transporting polypeptide (OATP) [3]

Grapefruit juice also inhibit P-glycoprotein, a transporter that carries drug from the enterocyte back to the gut lumen, resulting in a further increase in the fraction of absorbed drug [5,6,9].

Inhibition of P-glycoprotein is a possible mechanism that increases oral drug bioavailability by reducing intestinal efflux transport [6].

The compounds responsible for this interaction could result from a complex synergy among flavonoids (naringin, naringenin), furanocoumarins (6',7'-dihydroxybergamottin, bergamottin) and sesquiterpen (nootkatone) [5,10,11]. The compound may vary depending on the variety, maturity and origin of the fruit, local climatic conditions and the manufacturing process.

A single normal amount (e.g. 200-300 mL) or by whole fresh fruit segments can inhibit drug metabolizing enzymes, can increase oral bioavailability of a drug and enhance its adverse effects [5,6]. Enhanced oral drug bioavailability can occur 24 hours after juice consumption as the duration of effect of grapefruit juice can last 24 hours [6,11]. These interactions appears to be influenced by individual patient susceptibility, type and amount of grapefruit juice and administration-related factors [11]. Therefore patients should take their medications at least 4 hours

distant from fruit juice intake [8].

DRUG INTERACTIONS

Grapefruit has high antioxidant activity. It contains lycopene, limonoids which appears to have anti-tumor activity. It can reduce blood levels of LDL and triglycerides as well [14].

Substances in grapefruit can change the metabolism of drug and increase the amount of medication that enters the bloodstream to dangerous levels. The amount of drug metabolizing enzymes may varies from person to person. So grapefruit juice may affect people differently [15]. Table-1 shows possible drug interaction of Grapefruit juice.

CONCLUSIONS

Drug-fruit juice interactions have remained an active area of research. Though grapefruit provides health benefits, it can alter metabolism of many drugs. So it is wise, to consult with a physician or pharmacist and read medication guide or patient information sheet, that present in medicine box before taking medicine.

Food	Mechanism / effects / caution	Drugs considered for interaction with Grapefruit juice
Grapefruit juice	Grapefruit juice is an enzyme inhibitor and inhibit metabolism of concomitantly used drugs and increases their plasma concentration	<p><u>Cardiovascular drugs</u> Antiarrhythmics: amiodarone, dronedarone Calcium channel blockers: amlodipine, felodipine, Isradipine, lacidipine, lercanidipine, nicardipine, nifedipine, nimodipine and verapamil Ivabradine Lipid regulating drugs: atorvastatin, simvastatin Ranolazine Drugs used in erectile dysfunction: sildenafil, tadalafil, vardenafil Tolvaptan <u>Antimicrobials</u> Antimalarials: artemether with lumefantrine Antivirals: efavirenz <u>Central nervous system drugs</u> Antidepressants: sertraline Antipsychotics: quetiapine Anxiolytics & Hypnotics: midazolam, buspirone <u>Immunosuppressants and anticancer drugs</u> Cyclosporin Cytotoxics: axitinib, bosutinib, crizotinib, vinflunine Sirolimus Tacrolimus <u>Antihistamine</u> Rupatadine <u>Miscellaneous drugs</u> Colchicine Ivacaftor</p>
Grapefruit juice	Grapefruit juice reduces plasma concentration of concomitantly used drugs	<p><u>Cardiovascular drugs</u> Aliskiren <u>Antihistamine</u> Bilastine</p>
Grapefruit juice	Avoid concomitant use	<p><u>Antimicrobials</u> Antimalarials: piperazine with artemimol <u>Immunosuppressants and anticancer drugs</u> Cytotoxics: everolimus, lapatinib, nilotinib, pazopanib <u>Miscellaneous drugs</u> Pirfenidone Ulipristal</p>

Table 1: Summary of possible drug interactions of Grapefruit juice [12].

REFERENCES

- [1]. Morton, J. Grapefruit. In: Fruits of warm climates. Julia F. Morton. Miami, FL;1987.p.152–158.
- [2]. Mertens-Talcott SU, Zadezensky I, De Castro WV, Derendorf H, Butterweck V. Grapefruit-drug interactions: can interactions with drugs be avoided? *J Clin Pharmacol*. 2006 Dec;46(12):1390-416.
- [3]. Bressler R. Grapefruit juice and drug interactions. Exploring mechanisms of this interaction and potential toxicity for certain drugs. *Geriatrics*. 2006 Nov;61(11):12-8.
- [4]. An G, Kaur Mukker J, Derendorf H, Frye RF. Enzyme- and transporter-mediated beverage-drug interactions: An update on fruit juices and green tea. *J Clin Pharmacol*. 2015 Jun 10.
- [5]. Lohezic-Le Devehat F, Marigny K, Doucet M, Javaudin L. Grapefruit juice and drugs: a hazardous combination?. *Therapie*. 2002 Sep-Oct;57(5):432-45.
- [6]. Bailey DG, Dresser GK. Interactions between grapefruit juice and cardiovascular drugs. *Am J Cardiovasc Drugs*. 2004;4(5):281-97.
- [7]. Seden K, Dickinson L, Khoo S, Back D. Grapefruit-drug interactions. *Drugs*. 2010 Dec 24;70(18):2373-407.
- [8]. Andrade C. Fruit juice, organic anion transporting polypeptides, and drug interactions in psychiatry. *J Clin Psychiatry*. 2014 Nov;75(11):e1323-5.
- [9]. Palumbo G, Bacchi S, Palumbo P, Primavera LG, Sponta AM. Grapefruit juice: potential drug interaction. *Clin Ter*. 2005 May-Jun;156(3):97-103.
- [10]. Shirasaka Y, Shichiri M, Mori T, Nakanishi T, Tamai I. Major active components in grapefruit, orange, and apple juices responsible for OATP2B1-mediated drug interactions. *J Pharm Sci*. 2013 Jan;102(1):280-8. doi: 10.1002/jps.23357. Epub 2012 Nov 6.
- [11]. Arayne MS, Sultana N, Bibi Z. Grape fruit juice-drug interactions. *Pak J Pharm Sci*. 2005 Oct;18(4):45-57.
- [12]. BMA & Royal Pharmaceutical Society. Appendix-1: Interactions. *British National Formulary* 2014;67: 917-918.
- [13]. <https://www.google.com/search> (Date 18/08/15)
- [14]. http://www.whfoods.com/gen_page.php? tname =foodspice &dbid=25 (Date 18/08/15)
- [15]. <http://www.fda.gov/downloads/forconsumers/consumerupdates/ucm292839.pdf> (Date 18/08/15)

How to cite this article:

Sujit Kumar Sarker, Khin Darli Tun, Eliza Omar Eva, Ratna Paul. Grapefruit Juice: Nutritional Values and Drug Interactions: A Review. *Int J Intg Med Sci* 2015;2(10):186-189. DOI: 10.16965/ijims.2015.134