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Review Article

# Evidence for the effectiveness of pomegranate supplementation for blood pressure management is weak: A systematic review of randomized clinical trials



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ABSTRACT

Hypertension is one of the most important preventable causes of premature death. Studies have been conducted assessing the impact of pomegranate on blood pressure, with varying results. The aim of this review was to critically appraise and evaluate the effect of pomegranate on blood pressure in adults, using evidence from randomized clinical trials (RCTs). We conducted electronic searches in Medline, Embase, Amed, and The Cochrane Library, and included RCTs assessing the effectiveness of pomegranate on blood pressure. We assessed the reporting quality using the Cochrane criteria. We included 8 RCTs comprising 619 participants. The studies varied in their reporting quality, and compared pomegranate juice or capsules with a control. Two studies reported significant reductions in systolic blood pressure favoring pomegranate:  $p = .002$  and  $p < .001$  respectively; 3 studies reported no significant differences between groups; and 3 studies failed to report between-group differences. Two studies reported significant reductions in diastolic blood pressure favoring pomegranate:  $p = .038$ ,  $p < .001$ , respectively; 4 studies reported no significant between-group differences; and 2 studies did not report between group differences. No adverse events were observed. The limited evidence from clinical trials to date fails to convincingly show a beneficial effect of pomegranate on blood pressure. We have identified evidence gaps and highlight areas for future research to be conducted, including performing studies of high quality and longer duration.

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## 1. Introduction

Hypertension is a major risk factor for cardiovascular disease and one of the most important preventable causes of premature morbidity and mortality [1]. Clinical management of hypertension is one of the most common interventions in primary care, accounting for approximately £1 billion in drug costs annually in the UK alone [1]. Hundreds of dietary supplements are currently marketed for the management of hypertension, but the evidence for their effectiveness is mixed [2]. One such supplement presently promoted for CVD management is pomegranate.

Pomegranate, *Punica granatum*, is a fruit-bearing shrub native to the Middle East [3], but is cultivated in several regions globally [4]. The fruit is widely touted as a functional food and commonly used as a supplement in various forms [5]. Pomegranate peel is also used as a food preservative [6]. Phytochemically, pomegranate possesses high polyphenolic content [7], and this property has been utilized in the prevention and/or treatment of various medical conditions including diabetes [8], cardiovascular disease (CVD), cancer [9], and osteoporosis [10].

Pomegranate decreases lipid peroxidation and protein oxidation, increasing the concentration of glutathione (GSH), and enhancement of nitric oxide activity [11,12]. These antioxidant actions have been reported to be responsible for its purported protective effects against atherosclerosis [13,14]. Results of animal research have suggested that pomegranate juice inhibits angiotensin converting enzyme (ACE) [15,16], and in humans consumption of pomegranate juice reduces the activity of ACE by as much as 36%, leading to reductions in systolic blood pressure [17].

Pomegranate is usually marketed either as juice, syrup concentrate, or pills. Several clinical trials of pomegranate on blood pressure have been conducted; however, the results of these have not been systematically reviewed. Therefore, the objective of this review was to systematically appraise and evaluate the evidence from randomized clinical trials (RCTs) investigating the effects of pomegranate consumption on blood pressure in adults.

## 2. Approach

### 2.1. Search strategy

We conducted electronic searches on the following databases: MEDLINE, Embase, AMED, and The Cochrane Library. Each database was searched from inception up to October, 2016. Search terms used included pomegranate, *Punica granatum*, blood pressure, and derivatives of these [see web appendix A for the full MEDLINE search strategy]. No time or language restrictions were imposed. We also searched Google Scholar for relevant internet proceedings, and we hand searched the bibliography of located articles. No time or language restrictions were imposed.

### 2.2. Eligibility criteria and study selection

Included RCTs had to test the effect of pomegranate juice, extract or capsules on blood pressure in subjects aged 16 years and above and lasted at least 2 weeks. RCTs were included irrespective of lifestyle modification incorporated into the trial regimen. The included studies needed to report blood pressure as an outcome measure. Studies in which pomegranate was combined with other types of dietary supplements were excluded.

The primary outcomes were systolic and diastolic blood pressure. Our secondary outcome was adverse events. Data from each study was extracted according to participant characteristics, type of intervention and comparator, and results. Two reviewers [OAG and IJO] independently extracted the data, with disagreements resolved through discussion.

### 2.3. Quality assessment

The reporting quality of all included studies was assessed using the Cochrane risk of bias criteria [18] which examines the following domains: method of randomization, concealment of allocation, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data

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