Berberis vulgaris for cardiovascular disorders: a scoping literature review

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ABSTRACT

Cardiovascular disorders are the leading cause of mortality worldwide. Berberis vulgaris (B. vulgaris) is a commonly used plant in traditional medicine. In recent studies, B. vulgaris showed antiarrhythmic, antihypertensive, anticholinergic, and cardioprotective effects. We reviewed the literature to explore the possible prophylactic and therapeutic roles of B. vulgaris in cardiovascular medicine. A computer literature search was conducted to identify all relevant studies that have investigated the role of B. vulgaris in prevention or treatment of cardiovascular diseases. We also searched the citations of the retrieved articles. Using a systematic approach, we conducted a scoping review that included a total of 37 articles. Twelve studies examined the antihypertensive effects of B. vulgaris, seven studies investigated its antiarrhythmic effects, while its inotropic and cardioprotective effects were evaluated in four and eight studies, respectively. B. vulgaris showed a beneficial effect in reducing blood pressure, enhancing cardiac contractility, and protection from reperfusion injury. However, the mechanisms of these effects are still under investigation. Moreover, it could modify major risk factors for cardiovascular disorders, such as oxidative stress, hyperglycemia, and hyperlipidemia. Further studies are needed to translate these findings into effective cardiovascular medications.

Introduction

Cardiovascular disorders are the leading cause of morbidity and mortality worldwide (1). According to the American heart association (AHA), about 16.5% of the global mortality can be attributed to hypertension, of which 45% are caused by coronary heart disease (2). Most of these disorders are untreatable and the current pharmacological strategies only aim at disease control (3). Adding to this, various biochemical compounds, especially those used in the treatment of arrhythmia and heart failure, have serious adverse events. Therefore, there is a growing trend towards using medicinal plants in health care generally and cardiovascular medicine, in particular (4).

Berberis vulgaris (B. vulgaris) is a shrub of the plant family Berberidaceae that grows in northwest Africa, western Asia, central, and southern Europe. Its fruit is an oblong red berry that ripens in late summer and autumn. It has obovate leaves and pendulous yellow flowers (5). It contains multiple phenolic compounds, organic acids, flavonoids (anthocyanins), protoberberines, and alkaloids, to which its biological activities are attributed (Figure 1) (4).

For 3000 years in traditional medicine, B. vulgaris has been used to stop chronic bleeding, relieve arthralgia, fight infections, and treat urinary stones due to its diuretic effect (6). Therapeutic uses of B. vulgaris have been a focus for experimental research.

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recently. Both animal and human trials have concluded that its extracts may have antioxidant (7, 8), anti-inflammatory (9), anti-mutagenic, antimicrobial, and anti-parasitic activities (10). It has also been tested for the management of chronic cholecystitis, non-alcoholic fatty liver disease (11), osteoarthritis, and other rheumatoid disorders (12). Its fruit is safe for human intake and has been approved by the FDA (13).

In cardiovascular medicine, *B. vulgaris* and its active constituents showed antiarrhythmic, anti-hypertensive, anticholinergic, anti-inflammatory, and cardioprotective effects from ischemia/reperfusion (I/R) injury (14, 15). Despite its numerous applications, the mechanism of action for most of its effects is not yet clear (4). This review explores the potential role of *B. vulgaris* in prevention or treatment of cardiovascular disorders.

## Materials and Methods

### Data sources

We performed a computer literature search of the following authentic databases: PubMed, Persian Electronic Scientific Information Database (SID), Iranmedex, and Natural Medicines Comprehensive Database for all preclinical and human studies of *B. vulgaris* in cardiovascular medicine, using the search terms “Barbery”, “Berberis vulgaris”, “Berberine”, “Berbamime”, “Cardiovascular”, “Heart”, and “Hypertension”. We also searched the reference list of retrieved records for any relevant studies.

### Study selection

We included original studies of all designs, including preclinical (in vivo and in vitro) and human studies provided that they evaluated the prophylactic or therapeutic roles of *B. vulgaris* or its active constituents in cardiovascular medicine. We excluded secondary reports (literature reviews, systematic reviews, or meta-analyses) and non-English articles. Two authors independently reviewed the titles and abstracts of the search results and if the abstract was not conclusive, the full text was obtained to make a cut-off decision.

### Results

Our search strategy retrieved 721 records. After abstract and full-text screening, we included 33 full-text articles. An additional four articles were retrieved by screening the reference list of included articles. Details of our literature search and screening process are illustrated in Figure 2.

### Antihypertensive effects

Several in vitro and animal studies have shown an antihypertensive effect for *B. vulgaris*. However, the mechanisms and vascular sites for this effect are still debatable. Fatehi et al reported that the immediate reduction of blood pressure after *B. vulgaris* intake can be attributed to modulation of both cardiac and vascular contractility (16, 17). In vitro studies have shown that pretreatment of isolated aortic rings and mesenteric vascular beds with *B. vulgaris* extract decreases their contractile response to phenylephrine administration. This effect may be attributed to alpha-adrenoreceptor antagonism (18). Moreover, the augmentation of K+ currents through activation of 4-aminopyridine-sensitive K+ channels and the inhibition of intracellular Ca2+ release from caffeine-sensitive pools can initiate relaxation of vascular smooth muscles and vasodilatation (19–22). Animal studies have also suggested a central nervous mechanism for *B. vulgaris* antihypertensive effect, based on the observation of parallel reduction of blood pressure and heart rate (17). Other mechanisms have been suggested as inhibition of angiotensin-convertase enzyme and direct release of NO/cGMP from rat aortic rings (19) and the potentiation of acetylcholine (23).

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**Figure 2.** A summary of the search and article selection process
Although its effects were widely studied in systemic hypertension, few studies have investigated the possible therapeutic effect of *B. vulgaris* extract in pulmonary hypertension. Mahdavi et al showed that *B. vulgaris* extract can be as effective as sildenafil in reducing right ventricular systolic pressure and right ventricular hypertrophy in monocrotaline-induced pulmonary hypertension (24).

**Antiarhythmic effects**

Several animal studies have shown that the active compounds from *B. vulgaris* extracts can have antiarrhythmic properties, such as prolonging the action potential duration (APD), increasing the atrial refractory period, and suppression of delayed afterdepolarization (30, 31). Berberine has been suggested to act as a class Ia or III antiarrhythmic agent. *In vitro* studies reported different possible mechanisms for the observed effects of berberine, such as K+ channels blockade (32, 33), decreasing Na+ influx (30), and increase of [Ca2+]i (34). Berberine can indirectly supplement anti-arrhythmic drugs by its inhibitory effect on the human CYP3A4 enzyme, through which many of these drugs are metabolized, increasing their potency. However, this interaction may require adjusting the anti-arrhythmic dosage and should be prescribed by a specialist (35).

In a clinical study by Zeng and Li, in patients with congestive heart failure (CHF), berberine reduced the frequency of ventricular premature complexes and increased the left ventricular ejection fraction (EF) (36). Other pharmacological studies have shown that it can prevent the development of ventricular fibrillation (VF) due to its inhibitory effect on K+ channels (32, 33). Although berberine has not been tested in large-scale clinical studies, the existing body of literature shows a great potential for this compound as a future anti-arrhythmic drug.

| Study ID       | Active constituent | Study design/animal model | Findings                                                                 |
|---------------|--------------------|--------------------------|-------------------------------------------------------------------------|
| Mahdavi et al 2016 (24) | *B. vulgaris* crude extracts | Rats (*in vivo*) | *B. vulgaris* crude extract (200 mg) or sildenafil significantly reduced the right ventricular systolic pressure, right ventricular hypertrophy (stimulated by monocrotaline-induced pulmonary hypertension). However, none of them had a significant effect on the plasma level of endothelin-1 or the lung tissue level of glutathione peroxidase and malondialdehyde. |
| Lee et al 2006 (25)  | Berberine         | Rats (*in vivo* and *in vitro*) | Berberine inhibited angiotensin II and hepargin-binding epidermal growth factor (HB-EGF) mediated vascular smooth muscle cell migration and proliferation *in vitro*. It also improved neointima formation *in vivo*. This effect is mostly mediated through suppression of the Akt (protein kinase B) pathway. |
| Fatehi et al 2005 a, b (16, 17) | *B. vulgaris* crude extracts | Rats (*in vivo* and *in vitro*) | *B. vulgaris* crude extract reduced the heart rate and the mean arterial pressure in hypertensive rats in a dose-dependent manner. Adding its extracts to isolated rat aortic rings and mesenteric beds reduced the contractile response, induced by phenylephrine. |
| Kang et al 2002 (19) | Berberine         | Rats (*in vitro*) | Berberine-induced vasodilatation of rat aorta, most probably through angiotensin converting enzyme-inhibitory activity and direct release of NO/cGMP from rat aortic rings. |
| Ko et al 2000 (21)  | Berberine         | Rats (*in vitro*) | Berberine reduced the contractile response of vascular smooth muscle to phenylephrine. Interestingly, removal of the endothelium attenuated the berberine-induced effect. This suggests that the vasodilator effect of berberine can be mediated through both endothelial and smooth muscle cells. |
| Marin-Neto et al 1998 (26) | Berberine | Human trial | In a clinical trial on 12 patients with congestive heart failure, berberine could reduce pulmonary and peripheral vascular resistance, increase left ventricular ejection fraction, and improve cardiac performance as measured by echocardiography. |
| Wong 1998 (27) | Berberine         | Rats (*in vitro*) | The vasodilator effect of low concentrations of berberine is solely endothelium-dependent, while high concentrations of berberine cause vasodilatation, irrespective of the endothelium state. |
| Olmez and Ilhan 1992 (18) | Berberine | Rats and rabbits (*in vitro*) | Berberine-induced vasodilatation of rat and rabbit aorta, most probably through α1-adrenoceptor antagonism. It also inhibited the contractile response of the aorta to norepinephrine and phenylephrine exposure. |
| Bova et al 1992 (28) | Berberine | Guinea pig (*in vitro*) | Berberine inhibited the aortic contractile response to norepinephrine and histamine, but this effect is unlikely to be mediated through voltage-gated calcium channels. |
| Chiou et al 1991 (29) | Berberine         | Rats (*in vitro*) | Berberine-induced vasodilatation of the rat mesenteric artery (Directly by inhibiting Ca2+ release from internal stores and indirectly by releasing endothelial derived relaxing factor [EDRF]) |
| Chun et al 1979 (23) | Berberine         | Rats (*in vivo*) | Berberine intravenous infusion lowered the blood pressure and the heart rate of rats, most probably through inhibition of true cholinesterase and potentiation of acetylcholine levels. |
**Cardioprotective effects**

Ischemic preconditioning (IPC) is a powerful adaptive response to protect the heart from subsequent ischemic damage (39). Ischemia/Reperfusion injury is thought to be mediated through intracellular Ca\(^{2+}\) overload due to the reduced activity of sarcoplasmic reticulum Ca\(^{2+}\)ATPase, leading to contractile dysfunction and activation of lytic proteases, such as calpain, which digest cytoskeleton and myofilament proteins including troponin I and T (40, 41).

Several studies have discussed the cardioprotective effects of berberine; however, its mechanism is still under investigation (4). It is suggested that berberine inhibits calpain by maintaining Ca\(^{2+}\) homeostasis.

Another suggested mechanism is the activation of phosphoinositide-3 kinase and protein kinase B enzymes, leading to inhibition of the glycosynthetic kinase-3β (GSK 3β) and opening the mitochondrial ATP-sensitive K channels (mitoKATP) (42). Zhang *et al.* noticed that low concentrations (10-100 nmol/L) of berberine improve post-ischemic cardiac function in a concentration-dependent manner. However, that effect diminished with higher concentrations of 300 nmol/L in Langendorff-perfused rat hearts and 100 nmol/L in isolated cardiac cells (32).

Other studies have shown that berberine can also prevent cardiac hypertrophy in rats that were exposed to high doses of L-thyroxine or underwent surgical binding of the aorta. Possible mechanisms are elevating cardiac NO content, Na\(^{+}K\) ATPase and Ca\(^{2+}\) ATPase activities, as well as decreasing plasma levels of norepinephrine and controlling the sympathetic tone (43, 44).

**Table 2. Summary of the findings of preclinical and clinical studies that investigated the antiarrhythmic effects of *Berberis vulgaris* extracts**

| Study ID          | Active constituent | Animal models     | Findings                                                                 |
|-------------------|--------------------|-------------------|--------------------------------------------------------------------------|
| Li *et al.* 2001  | Berberine          | Rats (*in vitro*) | Berberine prolonged action potential duration (APD) and blocked the inward rectifier K\(^{+}\) current and the outward delayed rectifier K\(^{+}\) current. Therefore, the antiarrhythmic mechanism of berberine is related to its inhibitory effects on inward and outward K\(^{+}\) currents. Berberine inhibited both L-type and T-type calcium channels in isolated guinea pig ventricular myocytes in a concentration-dependent manner. Berberine prolonged the repolarization phase of AP by inhibiting the delayed rectifier K\(^{+}\) currents and increasing the L-type Ca\(^{2+}\) currents (I\(_{\text{L}}\)). |
| Xu *et al.* 1997  | Berberine          | Guinea pig        | Berberine increased the APD in a concentration-dependent manner in isolated guinea pig ventricular myocytes. Berberine prolonged the repolarization phase of AP by inhibiting the delayed rectifier K\(^{+}\) currents and increasing the L-type Ca\(^{2+}\) currents (I\(_{\text{L}}\)). |
| Li and Wang 1997  | Berberine          | Rats (*in vitro*) | Berberine increased the APD in a concentration-dependent manner in isolated guinea pig ventricular myocytes. Berberine prolonged the repolarization phase of AP by inhibiting the delayed rectifier K\(^{+}\) currents and increasing the L-type Ca\(^{2+}\) currents (I\(_{\text{L}}\)). |
| Wang and Zheng 1997 | Berberine          | Guinea pig        | Berberine increased the APD in a concentration-dependent manner in isolated guinea pig ventricular myocytes. Berberine prolonged the repolarization phase of AP by inhibiting the delayed rectifier K\(^{+}\) currents and increasing the L-type Ca\(^{2+}\) currents (I\(_{\text{L}}\)). |
| Chi *et al.* 1996 | 8-oxyberberine (JKL1073A) | Canine            | Berberine increased the APD in canine Purkinje and ventricular muscle in a concentration-dependent manner (3 to 30 μm), without influencing other parameters of AP. It also reduced the sinoatrial spontaneous frequency. This means that berberine exerted class III antiarrhythmic and proarrhythmic actions in the cardiac muscle of dogs in *vitro*. |
| Wang *et al.* 1994 | Berberine          | Rats (*in vitro*) | Berberine possesses an antiarrhythmic activity via suppression of delayed afterdepolarizations (suppressed amplitude at 3 μm and suppressed frequency at 1 mg/kg), which is likely due to the reduction of Na\(^{+}\) influx. |
| Shaffer 1985      | Berberine          | Rats (*in vitro*) | In spontaneously beating rat atria, berberine (1 x 10\(^{-3}\) -3 x 10\(^{4}\) M) caused bradycardia, which was not prevented by atropine. It also had a positive inotropic effect by enhancing both the force-velocity relationship and the duration of the active state. The mechanisms for these actions may include an alteration in the trans-sarcolemmal flux of calcium and inhibition of intracellular calcium sequestration system. |

**Table 3. Summary of the findings of preclinical studies that investigated the cardioprotective effects of *Berberis vulgaris***

| Study ID          | Active constituent | Animal/ cellular models | Findings                                                                 |
|-------------------|--------------------|-------------------------|--------------------------------------------------------------------------|
| Tanabe *et al.* 2005 | Berberine          | Rats (*in vivo*)        | Berberine and cotinine showed antiproliferative effects against vascular smooth muscle cells (VSMCs) by blocking the cell cycle at G1 and G2/M phases. This effect was mediated through a selective reduction in the cyclin D1 protein through accelerated proteolysis. |
| Yang *et al.* 2004 | Berberine          | Rats (*in vivo*)        | Berberine prevented cardiac hypertrophy, induced by L-thyroxine, in rats through elevating cardiac NO content, Na\(^{+}K\) ATPase activity, and Ca\(^{2+}\) ATPase activity. |
| Hong *et al.* 2003 | Berberine          | Rats (*in vivo*)        | In rats with cardiac hypertrophy, berberine decreased the plasma levels of norepinephrine, controlled the total sympathetic tone, and inhibited the progress of cardiac hypertrophy. |
| Zeng *et al.* 2003 | Berberine          | Rats (*in vivo*)        | Berberine alleviated ischemia/reperfusion (I/R) injury and attenuated apoptosis in rat neonatal myocytes that were exposed to I/R. Berberine pretreatment of myocytes reduced lactate dehydrogenase (LDH) release and methyleneidoxaminohemate (MDA) formation in I/R groups, and inhibited apoptosis in ischemia and reperfusion groups. |
| Zhou *et al.* 2001 | Berberine          | Rats (*in vivo*)        | Berberine pretreatment significantly reduced the degree of verapamil-induced heart failure in the experimental group, compared to the control group. |
| Zhang *et al.* 1992 | Berberine          | Rats (*in vivo*)        | Berberine alleviated myocardial I/R injury through preservation of Na\(^{-}\)/K\(^{-}\) ATPase activity, attenuation of ischemia-induced Na\(^{+}\) overload and reperfusion-induced Ca\(^{2+}\) overload. Also, it reduced free radicals generation during reperfusion. |
| Li *et al.* 1991  | Berberine          | Rabbits (*in vitro*)   | Berberine (1 mumol/L) reduced the myocardial I/R damages and restored all parameters to the level of preischemia within 10 min of reperfusion. |
| Ren *et al.* 1995  | Berberine          | Human aortic intimal    | Administration of 30 to 100 μg/ml of berberine to a culture of human aortic intimal cells decreased |
Inotropic effects

Berberine is used in the East to treat CHF (46). Several studies have investigated the underlying mechanisms of the positive inotropic effect (PIE) of B. vulgaris extracts. Zhang et al. showed that the PIE of berbamine can be attributed to increasing myofilament Ca\(^{2+}\) sensitivity, thus avoiding the adverse events of several cardiotoxic agents that improve cardiac contractility through increasing intracellular Ca\(^{2+}\) concentration (50). Improving myofilament Ca\(^{2+}\) responsiveness can be explained by increasing cytosolic protein kinase C (an enzyme family that regulates cardiac contraction through controlling Ca\(^{2+}\) transients and myofilament Ca\(^{2+}\) sensitivity).

They also revealed that high concentrations of berbamine (300 nM) can be associated with a negative inotropic effect (NIE) through suppression of Ca\(^{2+}\) transients and cellular shortening, thus suggesting a biphasic concentration-dependent regulation of cardiac function (50). In another study by Li et al. (48), high concentrations of berbamine resulted in inhibition of cardiac muscle contraction in the isolated rabbit hearts. Moreover, berbamine and its active derivatives were proven to inhibit calmodulin at micromole concentrations (51, 52).

Antiplatelet effect

Few studies have reported a possible antiplatelet effect of B. vulgaris extracts and berberine, in particular. In a clinical study by Huang et al., using berberine increased thrombolysis, induced by plasminogen activators (53). Feng et al. reported that berberine could be more efficacious than aspirin in preventing platelet aggregation in patients with atherosclerotic cerebral infarction (54). In another study by Fukuda et al., berberine could directly inhibit different stages of platelet-dependent inflammatory processes in a dose-dependent manner (55).

Several mechanisms have been proposed for the observed antiplatelet effect of berberine, such as inhibition of arachidonic acid metabolism, reduction of thromboxane A2 release from platelets (56), delineation of the calcium influx (57) and the partial agonist effect on platelet \(\alpha_2\)-adrenoceptors (53, 58). However, the exact mechanism has not been fully uncovered. Further studies are warranted to understand the molecular mechanism behind this effect before translation into large randomized clinical trials.

Discussion

Our study adds to the literature by outlining the effects and mechanisms of B. vulgaris in cardiovascular medicine, making it a strong candidate for further clinical trials and human applications. The current literature suggests that B. vulgaris extracts can directly influence the cardiovascular system through their cardioprotective, inotropic, and antihypertensive effects. However, some of the mechanisms, underlying these effects, are still largely unknown and have not been tested in clinical trials due to lack of preclinical evidence. Figure 3 summarizes the mechanisms of B. vulgaris cardiovascular actions.

- **Table 4.** Summary of the findings of preclinical studies that investigated the inotropic effects of *Berberis vulgaris* extracts

| Study ID | Active constituent | Study Design/Animal model | Findings |
|----------|--------------------|---------------------------|----------|
| Zhang et al 2011 (50) | Berbamine | Rats (in vitro) | Berbamine increased myocardial contractility by increasing intracellular Ca\(^{2+}\) concentrations. It also enhanced myofilament Ca\(^{2+}\) sensitivity by increasing cytosolic protein kinase C (PKC) |
| Zeng and Li 2001 (36) | Berberine | Human trials | Berberine reduced the frequency of ventricular premature complexes and increased the left ventricular ejection fraction (EF) in patients with congestive heart failure |
| Hu et al 1992 (52) | Berbamine compound E6 | Rats (in vitro) | Berbamine compound E6 inhibited calmodulin-dependent myosin light chain kinase (MLCK) in a dose-dependent manner, an effect which was antagonized by the addition of more calmodulin. This suggests that berbamine has an inotropic effect by competitive antagonism with calmodulin |
| Xu 1986 (51) | 0-(4-ethoxy-butyl)berbamine (EBB) | Human trial | EBB had a more potent calmodulin antagonist activity than berbamine. This antagonism is competitive because it can be reversed by adding higher doses of calmodulin |

![Figure 3. Summary of the mechanisms of *Berberis vulgaris* cardiovascular actions](image-url)
Moreover, *B. vulgaris* extracts can protect against cardiovascular pathologies indirectly through targeting the associated risk factors. They exert a potent antioxidant activity through decreasing the formation of cellular thiobarbituric acid reactive species formation (TBARS) and nitric oxide (NO), as well as increasing the activity of glutathione peroxidase (GPx) and superoxide dismutase (SOD) (7, 8). There is a wealth of evidence regarding the hypoglycemic and hypolipemic properties of berberine. The hypoglycemic effect of berberine can be attributed to improving insulin sensitivity, inhibiting glucogenic enzymes, delaying carbohydrate absorption, and increasing cellular glucose uptake (59–61), while the hypolipemic effects are related to inhibiting adipogenesis and increasing LDL-C uptake by increasing its cellular receptors (62, 63). These effects can act in synergism with the direct cardiovascular effects of *B. vulgaris*.

The proven effects of berberine can have numerous applications, such as controlling stenosis after balloon angioplasty (25), replacing or supplementing antihypertensive and antiarrhythmic drugs, being an ideal drug for CHF due to its vasodilator, inotropic, and lusitropic effects (64). However, lack of evidence from randomized clinical trials limits the acceptability of the results from small clinical studies and further use in clinical practice (65).

**Dosage:** The therapeutic dose of *B. vulgaris*, used in most clinical situations, is about 200 mg for three to four times daily. Its extracts are standardized to contain 8% to 12% isoquinoline alkaloids (4). *B. vulgaris* extracts are widely available in the form of capsules, solutions, and topical preparations, such as ointments and tinctures. It can be used as a supplement for food and tea (66).

**Safety:** No toxic effects have been reported at doses used for clinical purposes. However, overdosage has been linked to vertigo, convulsion, nasal bleeding, kidney failure, skin and eye inflammation, and hypoglycemia (67). According to an animal study by Peychev, *B. vulgaris* is moderately toxic (LD₅₀ = 2.6 ± 0.22 g/kg body weight in mice). It is not recommended to exceed a daily dose of 500 mg (68).

According to a study by Arayne et al, *B. vulgaris* should not be used during pregnancy because it can cause uterine constriction, leading to miscarriage. Furthermore, large doses of berberine are warranted to have a teratogenic effect (69). *B. vulgaris* fruits contain dihydro-palmitinum hydroxide, which exerts anti-estrogen activities, causing endometrial atrophy and fetal malnourishment. Moreover, it should be avoided in jaundiced infants because it has bilirubin displacement properties (70). Despite the lack of clinical evidence, it is not recommended for use in infants below 2 years of age and elders over 65 years, as well as breastfeeding women (4). Individuals who suffer any organ dysfunction should only use it after medical consultation.

**Recommendations:** The mechanism of action and the bioactive components of these extracts need further exploration. Moreover, further information regarding dosage, duration, and pharmacokinetics are needed to optimize its pharmacological use. Larger clinical trials with longer follow-up periods are necessary to detect rare adverse events and investigate the long-term safety of *B. vulgaris* extracts. Randomized data about cost-effectiveness and quality of life, in comparison to the standard drugs of cardiovascular disorders, would be beneficial. Integrated use of *B. vulgaris* extracts with the current cardiovascular drugs should be considered and the possible interaction between these agents should be characterized. It is also essential to increase awareness of alternative medicine strategies among health care professionals to enable them to provide alternative treatments for their patients who are not responding or intolerant to current medications (71).

**Conclusion**

*B. vulgaris* showed a beneficial effect in reducing blood pressure, enhancing cardiac contractility, and protection from reperfusion injury. However, the mechanisms of these effects are still under investigation. Moreover, it can modify major risk factors for cardiovascular disorders, such as oxidative stress, hyperglycemia, and hyperlipidemia. Further trials are needed to translate these findings into effective cardiovascular medications.

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