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Review article

The benefits of coffee on skeletal muscle

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ABSTRACT

Coffee is consumed worldwide with greater than a billion cups of coffee ingested every day. Epidemiological studies have revealed an association of coffee consumption with reduced incidence of a variety of chronic diseases as well as all-cause mortality. Current research has primarily focused on the effects of coffee or its components on various organ systems such as the cardiovascular system, with relatively little attention on skeletal muscle. Summary of current literature suggests that coffee has beneficial effects on skeletal muscle. Coffee has been shown to induce autophagy, improve insulin sensitivity, stimulate glucose uptake, slow the progression of sarcopenia, and promote the regeneration of injured muscle. Much more research is needed to reveal the full scope of benefits that coffee consumption may exert on skeletal muscle structure and function.

Contents

1. Introduction

Coffee is the most consumed beverage in the world, behind water. It is estimated that 1.6 billion cups of coffee are consumed every day. Americans alone spend $40 billion on coffee each year. Thus, the impact of coffee consumption on health is of great interest. Fortunately, coffee consumption has been associated with a plethora of health benefits and reductions in the risk of several chronic diseases such as type 2 diabetes, Parkinson's disease, various cancers, coronary artery disease, cardiac arrhythmias, and stroke [11]. Studies have also suggested that coffee consumption can decrease the risk of suicide [17,19] with the relative risk of suicide decreasing by 13% for every cup of coffee consumed daily [19] and coffee drinkers have a lower risk of all-cause mortality [31]. With the plethora of health benefits of coffee and the number of studies published on the topic regarding various organ systems, relatively little attention has been given to the effects on skeletal muscle, despite the fact that skeletal muscle is the largest organ in the body and an endocrine organ secreting hundreds of peptides, myokines, which influence the progression of age-related diseases and systemic aging [5,34]. Thus, the focus of this review is the effects of coffee on the underappreciated organ system: skeletal muscle.

Coffee contains more than 1000 chemical components thus making it a complex mixture [25]. The type of coffee bean, the roasting process, and the brewing/boiling process can all affect the chemical composition of the coffee liquid consumed. Of the many components, caffeine and chlorogenic acids are two of the most abundant. Chlorogenic acids can be broken down into caffeic acid and quinic acids by the roasting process and gut microflora upon ingestion [25,49]. Coffee also contains beneficial micronutrients such as magnesium, potassium, vitamin E, and niacin. Other components include diterpenes, such as cafestol and kahweol, which are present in boiled coffee but mostly removed during the brewing process of filtered coffee [25]. These oils are effectively extracted by a paper filter during brewing. Diterpenes are thought to be the culprit for the association between coffee consumption and higher

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serum total and LDL cholesterol concentrations observed in some epidemiological studies, especially those consuming boiled coffee [11]. With all of the chemical components of coffee, it is likely that the mixture of these components is responsible for maximizing health benefits rather than any one individual component.

2. Benefits of coffee on skeletal muscle

Using animal and in vitro models, coffee has been shown to induce autophagy, stimulate glucose uptake, improve insulin sensitivity, slow the progression of sarcopenia, and stimulate regeneration of injured muscle. To date, there has been no studies investigating the effects of coffee on skeletal muscle mass, function, or cellular processes in humans, thus underscoring the need for such studies.

2.1. Effects of coffee on autophagy

Autophagy is an evolutionary conserved cellular process essential for health and longevity [40]. Autophagy is essential for degradation and recycling of cell components, such as long-lived proteins, organelles, and other cytoplasmic contents. Skeletal muscle has one of the highest basal rates of autophagy compared to other tissues which can be enhanced by various cellular stresses, such as starvation or exercise [29]. Autophagy is required for proper turnover and renewal of mitochondria, maintenance of muscle mass, muscle integrity, and plays a role in exercise-induced plasticity such as fiber-type shifting, enhanced insulin sensitivity, and prevention of mitochondrial damage during physical activity [23,42,44]. Mice deficient in autophagy develop severe muscle weakness, atrophy, and decreased muscle contractility [42]. It has also been shown that autophagy is deficient in aged muscle and may contribute to mitochondrial dysfunction, enhanced oxidative stress, and the decline of muscle homeostasis which occurs during the aging process [27].

The process of autophagy involves the formation of a double membrane phagophore, elongation into an autophagosome, engulfment of cargo, and fusion of the autophagosome with the lysosome (see Fig. 1)[9]. These steps are regulated by a large family of autophagy related (Atg) proteins. Furthermore, the process is regulated by nutrient sensors such as AMP-activated protein kinase (AMPK) and mammalian target of rapamycin complex 1 (mTORC1). When AMPK is stimulated, for example by rising levels of AMP, AMPK activates a number of processes, including autophagy, in order to elevate ATP content. AMPK induces autophagy via phosphorylation and inhibition of mTORC1. Two commonly used markers of autophagy are the generation of microtubule-associated protein light chain 3-II (LC3-II) from LC3 and degradation of sequestosome 1 (p62/SQSTM1). LC3-II plays a role in fusion of membranes and selection of cargo for degradation. Formation of LC3-II requires the cleavage of LC3 into LC3-I followed by conjugation to phosphatidylethanolamine to form LC3-II. p62/SQSTM1 is one of several proteins recruited to the outer mitochondrial membrane during autophagy/mitophagy which plays a role in perinuclear aggregation and clearance of damaged mitochondria via autophagosomes and, thus, is used as a marker of autophagic flux since it is degraded during this process [16]. p62/SQSTM1 has also been shown to interact with LC3 to facilitate degradation of ubiquitinated protein aggregates.

Coffee has been shown to induce autophagy in several tissues in vivo, including skeletal muscle [36]. Chronic consumption of coffee, diluted in the drinking water of female mice, stimulated autophagy in the liver, heart, and skeletal muscle in a dose-dependent manner, as evidenced by increased generation of LC3-II and enhanced degradation of p62/SQSTM1. These effects were first observed at 24 h post-treatment initiation and continued throughout the two-week experimental period. It was further determined that the induction of autophagy was associated with global protein lysine deacetylation and decreased phosphorylation of mTORC1. Moreover, it was determined that the activation AMPK was not associated with chronic coffee consumption, however AMPK was activated by acute coffee consumption. Thus, autophagy associated with chronic coffee consumption may result from deacetylation and activation of autophagic proteins as well as inhibition of mTORC1, rather than the activation of AMPK. (see Fig. 1).

Since caffeinated and decaffeinated coffee were both shown to stimulate autophagy, the authors concluded that the effects were independent of caffeine content [36]. It was suggested that the observed effects must be due to other components of coffee that are not removed during the decaffeination process, such as polyphenols. Indeed, polyphenols have been shown to induce autophagy, as well as proteome lysine deacetylation [33,37]. However, others have shown that caffeine, in vitro, can stimulate autophagy in C2C12 myoblasts via calcium-dependent activation of AMPK [28].

In summary, coffee may exert a positive impact on skeletal muscle, in part, by inducing autophagy. Upregulated autophagy may prevent the accumulation of damaged proteins and organelles which optimizes cellular function.

2.2. Effects of coffee on insulin sensitivity and glucose uptake in skeletal muscle

Epidemiological studies have shown a relationship between coffee consumption and reduced incidence of type 2 diabetes [1,13,46,47]. The incidence of type 2 diabetes has reached epidemic proportions

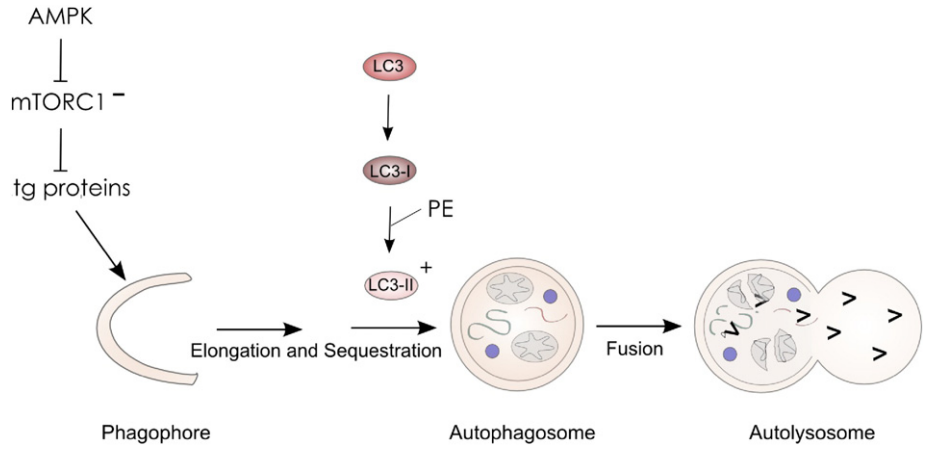

Fig. 1. Simplified scheme of autophagy and the effects of chronic coffee consumption. AMPK phosphorylates and inhibits mTORC1, which normally suppresses Atg proteins required for autophagy. LC3-II is required for formation of the autophagosome before fusion with the lysosome to form the autolysosome. Activation of LC3-II requires cleavage of LC3 into LC3-1 followed by conjugation to phosphatidylethanolamine (PE). Chronic coffee consumption stimulates the process of autophagy evident by increased (+) production of LC3-II and degradation of p62/SQSTM1 (not shown) which is associated with dephosphorylation and inhibition (−) of mTORC1. Arrows indicate stimulation; blunt ends indicate inhibition.