Overview: Edible Bird’s Nest (EBN) is one of the widely used health foods in Chinese traditional medicine. In this study the authors hypothesized that EBN extract may reduce the progression of osteoarthritis (OA) and help cartilage regeneration. Accordingly, they used an in vitro model and investigated the effects of EBN extract on the catabolic and anabolic activities of human articular chondrocytes isolated from knee joints of patients with OA. A single batch of EBN extract was prepared by extraction with hot water. After determining the optimum concentration for use on chondrocyte cultures using the MTT assay, the extract was used to study the effects of HMG on catabolic and anabolic gene expression in chondrocytes by using real-time PCR. Prostaglandin E2 (PGE2) production was determined by using an ELISA method and the total quantity of sulphated glycosaminoglycans (GAGs) produced by chondrocyte cultures was quantified by using the 1,9-dimethylmethylene blue (DMMB) assay. The authors suggest, based on the data presented, that EBN extract was able to reduce the expression of catabolic genes encoding matrix metalloproteinases (MMP-1 and MMP-3), cytokines (IL-1, IL-6 and IL-8) and other inflammatory mediators (COX-2 and iNOS) in cultured chondrocytes. PGE2 production was also reduced. EBN extract also increased expression of type II collagen, aggrecan and SOX-9 as well as sGAG production. The authors also propose that Edible Bird’s Nest extract demonstrates chondroprotective properties by reducing the expression of inflammatory mediators of cartilage destruction and increasing cartilage extracellular matrix synthesis. Based on the in vitro data presented the authors suggest that EBN extract is a potential agent for the treatment of OA.

Specific Comments: This is an interesting study but the paper is very poorly written and requires Major Compulsory Revisions. The authors are requested to use the services of a professional manuscript editing service to improve the English language and syntax in the manuscript. The comment regarding the English language relates to the entire manuscript. There are too many examples of poor English to list here in this review. The English language in the manuscript
text requires a complete overhaul.

Please see the comments below:

1. Title: the title is slightly misleading. The authors have studied EBN in the context of its action on primary chondrocytes from OA joints. The use of the work chondroprotective cannot really be justified in the title when studies are carried out on in vitro systems.

2. Abstract: the abstract is useful and clearly summarizes the work described. Please edit the abstract carefully for correct use of scientific English.

3. The introduction (background) appears to be too long. This reviewer proposes that 1.5 pages should suffice. The authors have written 3.5 pages. This section should be more focused and concise.

4. Methods: this reviewer has major concerns about extraction of EBN using hot water. What is the scientific rationale for this? Although EBN extracts are prepared by adding hot water in Chinese traditional medicine, this does not mean that it is the most valid method of extraction. The authors should discuss why methanol, ethanol, chloroform and DMSO were not used. The use of hot water for the extraction process needs to be fully justified. Also, the reasons for storage at 4 degrees centigrade should be clearly explained.

5. The authors have used chondrocytes from OA joints from 6 patients. This seems rather odd because the majority of investigators in this area of research use normal chondrocytes from HEALTHY and NORMAL JOINTS and subsequently stimulate them with pro-inflammatory cytokines to induce an OA-like environment in vitro. Why did the authors not use this standardized approach? OA is a very complex and heterogeneous disease and there are likely to be many differences between the chondrocytes isolated from OA joints of different patients. In terms of biological response and phenotype, each patient is likely to respond differently. There is no mention of the grade of OA in each of the samples used. How can the authors be confident that the cells isolated from 6 patients are homogeneous? This is a major criticism and needs to be addressed.

6. The MTT assay is not really a suitable assay because it is a proliferation assay rather than a viability assay. Why did the authors not use LIVE/DEAD assays or similar viability assays?

7. The discussion can be more focused and structured. The conclusion is clear and the authors have cited a reasonable number of references.

8. Tables 1 and 2 are clear.

9. The figures require significant improvements. The quality and resolution of all the figures presented is poor. The figures are not sharp enough and the files appear to be of very low resolution. The authors have clearly used Microsoft Excel for the figures. Microsoft Excel is not a scientific graphics package. It is primarily intended for use by the business and finance sectors. A scientific graphics package such as Minitab, SigmaPlot or GraphPad should be used instead.

10. The use of color is not scientifically justified in the graphs. There is no scientific reason for the control bars to be plotted in red.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

Declaration of competing interests:
I do not have any conflict of interest to declare.

Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this paper, either now or in the future?
No

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Do you have any other financial competing interests?
No

Do you have any non-financial competing interests in relation to this paper?
No