Reviewer #1:

The primary issue of this manuscript is that the authors focused on describing the content of the references, but they had few summary from their own perspectives. When quoting the original text, the authors should refine and summarize the content of the article rather than directly quoting the original sentence.

Ans: The content has been refined.

The authors should carefully check the use of abbreviations in the manuscript. Use the full name at its first occurrence, and then use its abbreviation. For example, in the "Conclusion" section, the authors said "...in this axis during the progression of hepatocellular carcinoma (HCC) are intricate", where the words "hepatocellular carcinoma (HCC)" should be revised as "HCC". The same mistakes can be easily seen.

Ans: On page no. 34 "hepatocellular carcinoma" has been omitted

Language and grammar should be improved. For example, in the "Introduction" section, the authors said "As transplantation, ablation and resection can only be used for the treatment of early-stage HCC patients and since diagnosis of the majority of patients is diagnosed with severe stages...", where the words "diagnosis of" should be deleted. The same mistakes can be easily seen.

Ans: On page no. 2 "diagnosis of" is omitted

In the "p53 alterations and hepatocarcinogenesis" section, the authors said "Aflatoxin B1, which contaminates foods in regions where it is endemic, clearly plays a part in the development of ss...", what's the meaning of "ss"?

Ans: On page no. 11 "ss" is replaced

In the "Aflatoxin B1 (AFB1)" part of "Roles of p53 in extrinsic factor-induced liver carcinogenesis" section, the authors said "As a result, the p53 mutation caused by AFB1 is critical for the development of HCC, pIt's interesting to note that HepG2 cell viability and proliferation are reduced when IGF-2 is silencedresumably through increased IGF-2 signalling.", where the words "pIt's" and "silenced resumably" were wrong.

Ans: On page no.12 correction has been done.

In the "Non-alcoholic fatty liver disease (NAFLD)" part of "Roles of p53 in extrinsic factor-induced liver carcinogenesis" section, the authors said "Just 11.5 per cent of individuals...", where the word "per cent" should be revised as "percent".

Ans: On page no. 14 correction has been done.

Reviewer #2:

In this study, The authors conducted a large number of literature research, not only analyzing the molecular mechanism of P53 on the development and progression of hepatocellular carcinoma, but also listing how P53 is involved in cancer formation under multifactorial conditions (aflatoxin, vinyl chloride, nonalcoholic fatty liver, iron overloading, hepatitis B virus, hepatitis C virus, etc.). In addition, the authors summarize P53 as a therapeutic target and what is said about drug resistance. Finally, it is proposed that future research directions should focus on the malfunction of the MDM2-P53 axis. In conclusion, the authors made a detailed review of the tumor suppressor gene P53. Although P53-related research has taken many years, its signal transduction pathway is complex and highly correlated with cancer occurrence, and it still has great research value. Therefore, this article has certain reference significance for guiding basic research. However, there are still some parts of the manuscript that need to be improved. 1. Language needs further improvement. There are still some statements that are difficult to understand. In the "Tumour Suppressor p53" section, the authors mentioned that "A variety of stress signals are detected by p53", such statements are obviously confusing. Moreover, there is no source of documentary evidence for this statement.

Ans: On page no. 5 the above statement is cited.

2. The penultimate line in the "Tumour Suppressor p53" section, "RINg finger domain" should be "RING finger domain". There are similar problems in the text, for example, in the "Non-alcoholic fatty liver disease (NAFLD)" section, there are some spelling mistakes, such as "percent" with a space in between, "NFk-B" should be written as "NF-κB".

Ans: On page no. 6 RING finger domain is corrected. On page no. 14 NF-kB is corrected.

3. The figure notes in this manuscript have too little descriptive text to introduce the content of the figures specifically.

Ans: On page no. 3, 6, 9 figure legend has been added.

4. The authors have already described the location of p53 in the chromosome and the size of its encoded in the first paragraph of "Tumour Suppressor p53" section, but then repeated this description in the last sentence of the first paragraph of "Role of p53 in mechanisms of hepatocarcinogenesis".

Ans: On page no. 8 changes has been done.

5. The pathogenesis of P53-associated HCC still needs to be elaborated in the context of specific biological phenomena and given an appropriate explanation. The connection and special features of P53 as a tumor target with other related biological targets need to be highlighted.

Ans: On page no. 7 the pathogenesis is added

Reviewer #3:

The authors systematically reviewed the role and mechanism of p53 in the pathogenesis of HCC and therapeutic strategy targeting p53. There are several comments:

1. The role of p53 in carcinogenesis and its regulation with MDM2 has already been reported. Several reviews have summarized similar content (PMID: 25477334, 32595984). In addition, references about p53 and HCC in recent years are rarely cited and presented in your article. It should be updated.

Ans: The stated changes has been amended.

2. In the section of 'Roles of p53 in extrinsic factor-induced liver carcinogenesis', alcohol and cirrhosis are very important factors promoting carcinogenesis, which should not be omitted. Please add it.

Ans: On page no. 13 and 20 the content is added.

3. In the section of 'Therapeutic products with p53 as a target', studies of therapeutic approaches targeting p53 are presented. However, these studies only stay at the cellular or animal model level. Is there any clinical trial of therapeutic agent targeting p53?

Ans: On page no. 29 the table of clinical trial is added.

4. The author summarized the role of p53 in resistance to several chemotherapeutic agents, cisplatin and doxorubicin. However, several important related studies in recent years (PMID: 31244936, 21660965, etc.) were not presented.

Ans: On page no. 32 the content is added.